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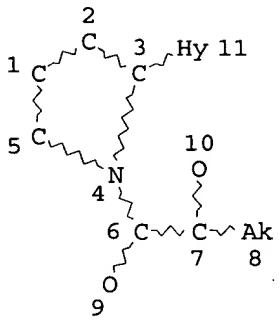
L1 HAS NO ANSWERS
L1 STR



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DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 11

STEREO ATTRIBUTES: NONE

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100.0% PROCESSED 52020 ITERATIONS 51 ANSWERS
SEARCH TIME: 00.00.01

L3 51 SEA SSS FUL L1

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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	140.66	140.87

FILE 'CAPLUS' ENTERED AT 15:15:10 ON 03 DEC 2002
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 3 Dec 2002 VOL 137 ISS 23
FILE LAST UPDATED: 2 Dec 2002 (20021202/ED)

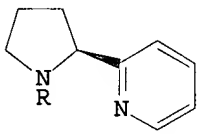
This file contains CAS Registry Numbers for easy and accurate substance identification.

CAS roles have been modified effective December 16, 2001. Please check your SDI profiles to see if they need to be revised. For information on CAS roles, enter HELP ROLES at an arrow prompt or use the CAS Roles thesaurus (/RL field) in this file.

=> s l3
L4 14 L3

=> d bib abs hitstr 14

L4 ANSWER 14 OF 14 CAPLUS COPYRIGHT 2002 ACS
AN 1991:163944 CAPLUS
DN 114:163944
TI Synthesis of 1-substituted 2-[(2S)-2-pyrrolidinyl]pyridine from L-proline
AU Chelucci, Giorgio; Falorni, Massimo; Giacomelli, Giampaolo
CS Dip. Chim., Univ. Sassari, Sassari, I-07100, Italy
SO Synthesis (1990), (12), 1121-2
CODEN: SYNTBF; ISSN: 0039-7881
DT Journal
LA English
OS CASREACT 114:163944
GI



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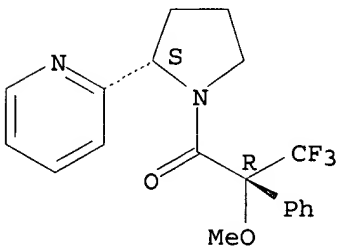
AB (.eta.5-Cyclopentadienyl)cobalt(1,5-cyclooctadiene)-catalyzed cyclotrimerization of (2S)-1-benzyloxycarbonyl-2-cyanopyrrolidine with HC.tplbond.CH in PhMe (14 bar, 110.degree., 22 h) gave title pyridine I (R = H). Alkylation of I (R = H) with HCHO/HCO2H gave 91% I (R = Me), whereas treatment with PhCH2Cl in DMF contg. Na2CO3-NaI gave 93% I (R = PhCH2).

IT **133031-60-4P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

RN 133031-60-4 CAPLUS
CN Pyrrolidine, 2-(2-pyridinyl)-1-(3,3,3-trifluoro-2-methoxy-1-oxo-2-phenylpropyl)-, [R-(R*,S*)]- (9CI) (CA INDEX NAME)

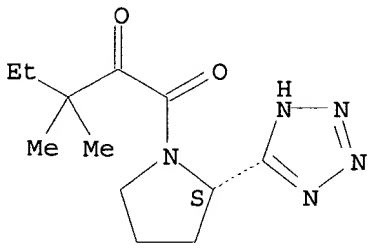
Absolute stereochemistry.



=> d hitstr 13

L4 ANSWER 13 OF 14 CAPLUS COPYRIGHT 2002 ACS
IT **222171-58-6P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(sensorineurotrophic compds., and prepn. thereof, for treating hearing loss)
RN 222171-58-6 CAPLUS
CN Pyrrolidine, 1-(3,3-dimethyl-1,2-dioxopentyl)-2-(1H-tetrazol-5-yl)-, (2S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



=> d bib abs hitstr 13

L4 ANSWER 13 OF 14 CAPLUS COPYRIGHT 2002 ACS
AN 1999:249062 CAPLUS
DN 130:262139
TI Method for treating hearing loss using sensorineurotrophic compounds
IN Magal, Ella
PA Amgen Inc., USA
SO PCT Int. Appl., 649 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 5

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9914998	A2	19990401	WO 1998-US19980	19980924
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
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	CA 2304647	AA	19990401	CA 1998-2304647	19980924
	AU 9895783	A1	19990412	AU 1998-95783	19980924
	AU 742040	B2	20011213		
	EP 1011650	A1	20000628	EP 1998-949467	19980924
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	JP 2001516767	T2	20011002	JP 2000-512395	19980924
PRAI	US 1997-59905P	P	19970924		
	US 1997-59963P	P	19970925		
	US 1998-159105	A	19980923		
	WO 1998-US19980	W	19980924		

OS MARPAT 130:262139

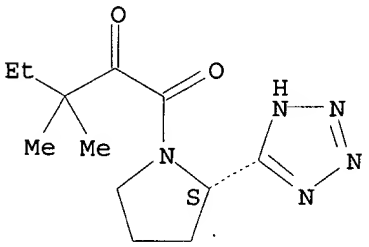
AB Methods are provided for preventing and/or treating injury or degeneration of inner ear sensory cells, e.g. hair cells and auditory neurons, by administration of a sensorineurotrophic compd. to a patient in need thereof. Compd. prepn. is included.

IT **222171-58-6P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(sensorineurotrophic compds., and prepn. thereof, for treating hearing loss)

RN 222171-58-6 CAPLUS

CN Pyrrolidine, 1-(3,3-dimethyl-1,2-dioxopentyl)-2-(1H-tetrazol-5-yl)-, (2S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



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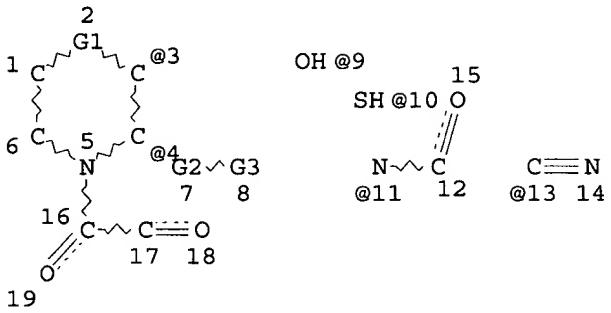
L1 STR



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VAR G3=9/10/11/13
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 19

STEREO ATTRIBUTES: NONE

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100.0% PROCESSED 52167 ITERATIONS 11 ANSWERS
SEARCH TIME: 00.00.07

L3 11 SEA SSS FUL L1

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=> s l3
L4            7 L3

=> d bib abs hitstr 1-7

L4   ANSWER 1 OF 7  CAPLUS  COPYRIGHT 2002 ACS
AN   2000:384175  CAPLUS
DN   133:30959
TI   Preparation of prolinylalkanediones and related compounds for treating
     neurological disease, vision disorders, and alopecia.
IN   Hamilton, Gregory S.; Norman, Mark H.; Wu, Yong-qian
PA   GPI Nil Holdings, Inc., USA; Amgen, Inc.
SO   PCT Int. Appl., 166 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 5
     PATENT NO.         KIND  DATE           APPLICATION NO.   DATE
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PI   WO 2000032588      A2    20000608       WO 1999-US28663   19991203
     WO 2000032588      A3    20010222
         W:  AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU,
             CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL,
             IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA,
             MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI,
             SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM,
             AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE,
             DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,
             CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
     US 6331537         B1    20011218       US 1999-453571    19991202
     BR 9916461         A     20010904       BR 1999-16461     19991203
     EP 1135370         A2    20010926       EP 1999-961930    19991203
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO
     NO 2001002765      A     20010720       NO 2001-2765      20010605
PRAI US 1998-204237     A     19981203
     US 1999-453571     A     19991202
     US 1998-87788P     P     19980603
     WO 1999-US28663    W     19991203
OS   MARPAT 133:30959
GI
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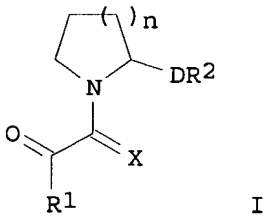


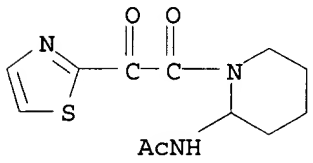
I

AB Title compds. [I; n = 1-3; X = O, S; R1 = (substituted) alkyl, alkenyl, aryl, heteroaryl, carbocyclyl, heterocyclyl; D = bond, (substituted) alkyl, alkenyl, alkynyl; R2 = CO2H, (substituted) CO2H isostere], were prepd. Thus, L-proline Me ester hydrochloride in CH2Cl2 was treated with Et3N and then with MeO2CCOCl to give 88% Me (2S)-1-(1,2-dioxo-2-methoxyethyl)-2-pyrrolidinecarboxylate. The latter in THF at -78.degree. was treated with 1,1-dimethylpropylmagnesium chloride followed by 3 h stirring at -78.degree. to give 75% Me (2S)-1-(1,2-dioxo-3,3-

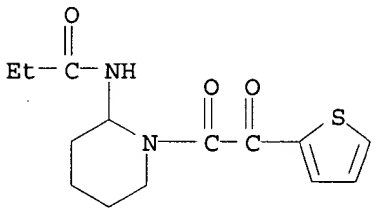
dimethylpentyl)-2-pyrrolidinecarboxylate. This was stirred overnight with aq. LiOH in MeOH to give 87% (2S)-1-(1,2-dioxo-3,3-dimethylpentyl)-2-pyrrolidinecarboxylic acid. In the MPTP model of Parkinson's disease in mice, I at 10 mg/kg orally gave 10.4-46.5% recovery of TH-stained dopaminergic neurons.

IT **251949-80-1P 251949-81-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of prolinylalkanediones and related compds. for treating neurol. disease, vision disorders, and alopecia)

RN 251949-80-1 CAPLUS
CN Acetamide, N-[1-(oxo-2-thiazolylacetyl)-2-piperidinyl]- (9CI) (CA INDEX NAME)



RN 251949-81-2 CAPLUS
CN Propanamide, N-[1-(oxo-2-thienylacetyl)-2-piperidinyl]- (9CI) (CA INDEX NAME)



L4 ANSWER 2 OF 7 CAPLUS COPYRIGHT 2002 ACS
AN 1999:784078 CAPLUS
DN 132:22860
TI Preparation of aza-heterocyclic compounds used to treat neurological disorders and hair loss
IN Hamilton, Gregory S.; Norman, Mark H.; Wu, Yong-Qian; Steiner, Joseph P.
PA Guilford Pharmaceuticals Inc., USA; Amgen, Inc.
SO PCT Int. Appl., 96 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 5

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9962881	A1	19991209	WO 1998-US25573	19981203
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2333963	AA	19991209	CA 1998-2333963	19981203

	AU 9917081	A1	19991220	AU 1999-17081	19981203
	ZA 9811063	A	20000707	ZA 1998-11063	19981203
	BR 9815920	A	20010220	BR 1998-15920	19981203
	EP 1084107	A1	20010321	EP 1998-961866	19981203
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	JP 2002516905	T2	20020611	JP 2000-552093	19981203
	NO 2000005903	A	20010202	NO 2000-5903	20001121
PRAI	US 1998-87788P	P	19980603		
	US 1998-101077P	P	19980918		
	WO 1998-US25573	W	19981203		

OS MARPAT 132:22860

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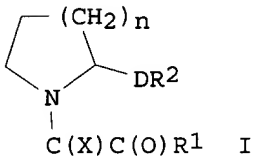


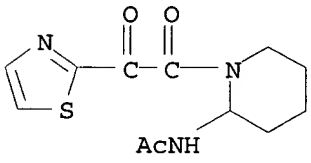
I

AB Prepn. of N-heterocyclic carboxylic acids and carboxylic acid isosteres I [n = 1-3; X = O, S; R1 = C1-C9 straight or branched chain alkyl, C2-C9 straight or branched chain alkenyl, aryl, heteroaryl, carboncycle, heterocycle; D = bond, C1-C10 straight or branched chain alkyl, C2-C10 alkenyl, C2-C10 alkynyl; R2 = carboxylic acid, carboxylic acid isostere] and their use for treating neurol. disorders and for treating alopecia and promoting hair growth are described. E.g., (2S)-1-(1,2-dioxo-3,3-dimethylpentyl)-2-hydroxymethylpyrrolidine was prepd.

IT **251949-80-1P 251949-81-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of aza-heterocyclic compds. used to treat neurol. disorders and hair loss)

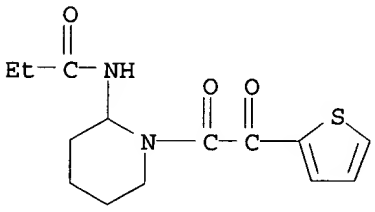
RN 251949-80-1 CAPLUS

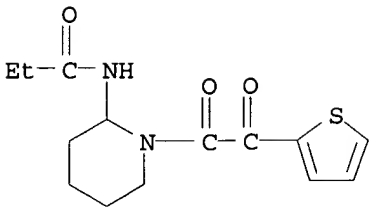
CN Acetamide, N-[1-(oxo-2-thiazolylacetyl)-2-piperidinyl]- (9CI) (CA INDEX NAME)



RN 251949-81-2 CAPLUS

CN Propanamide, N-[1-(oxo-2-thienylacetyl)-2-piperidinyl]- (9CI) (CA INDEX NAME)





RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 7 CAPLUS COPYRIGHT 2002 ACS
AN 1999:249062 CAPLUS
DN 130:262139
TI Method for treating hearing loss using sensorineurotrophic compounds
IN Magal, Ella
PA Amgen Inc., USA
SO PCT Int. Appl., 649 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 5

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9914998	A2	19990401	WO 1998-US19980	19980924
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
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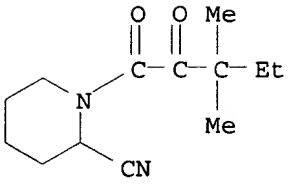
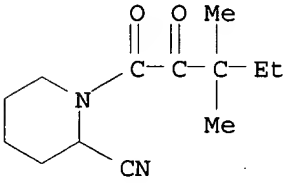
	CA 2304647	AA	19990401	CA 1998-2304647	19980924
	AU 9895783	A1	19990412	AU 1998-95783	19980924
	AU 742040	B2	20011213		
	EP 1011650	A1	20000628	EP 1998-949467	19980924
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	JP 2001516767	T2	20011002	JP 2000-512395	19980924
PRAI	US 1997-59905P	P	19970924		
	US 1997-59963P	P	19970925		
	US 1998-159105	A	19980923		
	WO 1998-US19980	W	19980924		

OS MARPAT 130:262139
AB Methods are provided for preventing and/or treating injury or degeneration of inner ear sensory cells, e.g. hair cells and auditory neurons, by administration of a sensorineurotrophic compd. to a patient in need thereof. Compd. prepn. is included.
IT **222171-50-8 222171-50-8D**, esters
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(sensorineurotrophic compds., and prepn. thereof, for treating hearing loss)
RN 222171-50-8 CAPLUS
CN 2-Piperidinecarbonitrile, 1-(3,3-dimethyl-1,2-dioxopentyl)- (9CI) (CA INDEX NAME)



RN 222171-50-8 CAPLUS
CN 2-Piperidinecarbonitrile, 1-(3,3-dimethyl-1,2-dioxopentyl)- (9CI) (CA INDEX NAME)



L4 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2002 ACS
AN 1997:473732 CAPLUS
DN 127:81793
TI Preparation of hydroxyethylamine core structures as HIV and FIV protease inhibitors
IN Wong, Chi-Huey; Slee, Deborah H.; Laslo, Karen
PA Scripps Research Institute, USA; Wong, Chi-Huey; Slee, Deborah H.; Laslo, Karen
SO PCT Int. Appl., 202 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9721100	A1	19970612	WO 1996-US19571	19961209
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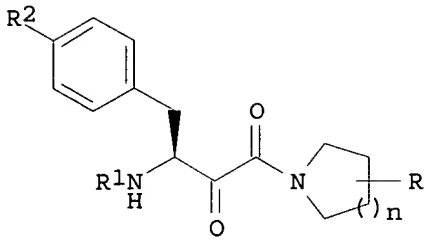
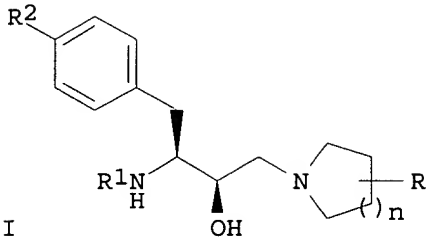
	AU 9712844	A1	19970627	AU 1997-12844	19961209
	AU 728373	B2	20010111		
	EP 873519	A1	19981028	EP 1996-943657	19961209
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	JP 2000502332	T2	20000229	JP 1997-521485	19961209
PRAI	US 1995-568532	A2	19951207		
	WO 1996-US19571	W	19961209		

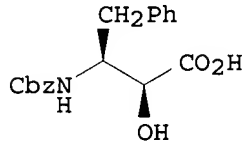
OS MARPAT 127:81793
GI



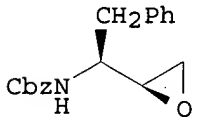
I



II



III



IV

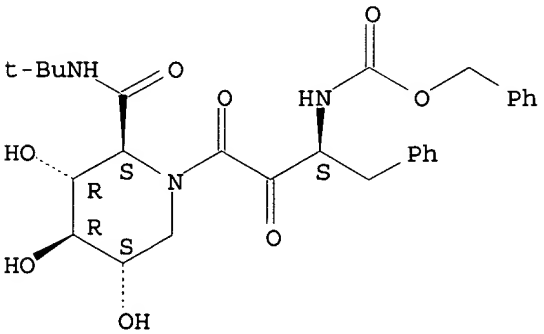
AB Combinatorial libraries of HIV and FIV protease inhibitors are characterized by .alpha.-keto amide or hydroxyethylamine core structures I and II [n = 1, 2; R = one or more groups CONHCMe3, CH2OH, CH2OMe, CH2OCH2Ph, OH, OCH2Ph, C1-4 alkoxy, optionally nitro-substituted 2-, 3-, or 4-MeOC6H4CH2O, 2,3- or 3,4-methylenedioxyphenylmethoxy, etc.; R1 = PhCH2O2C (Cbz), Me3CO2C (Boc), acyl; R2 = H, HO, PhCH2O, C1-4 alkoxy, optionally nitro-substituted 2-, 3-, or 4-MeOC6H4CH2O, 2,3- or 3,4-methylenedioxyphenylmethoxy] flanked by on one side by substituted pyrrolidines, piperidines, or azasugars and on the other side by Phe, Tyr, or substituted tyrosines. The libraries are synthesized via coupling of the nitrogen heterocycles with hydroxy acids, e.g. III, followed by oxidn. to the keto amide, or a one-step coupling with epoxides, e.g. IV. Highly efficacious drug candidates are identified by screening the libraries for binding and inhibitory activity against both HIV and FIV protease. Drug candidates displaying clin. useful activity against both HIV and FIV protease are identified as being potentially resistive against a loss of inhibitory activity due to development of resistant strains of HIV.

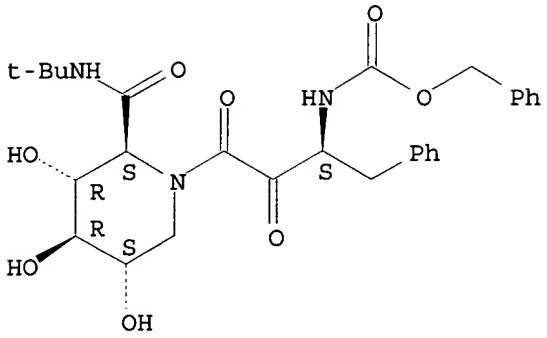
IT **191850-51-8P 191850-64-3P 191850-67-6P 191850-75-6P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of hydroxyethylamine core structures as HIV and FIV protease inhibitors)

RN 191850-51-8 CAPLUS

CN Carbamic acid, [3-[2-[[(1,1-dimethylethyl)amino]carbonyl]-3,4,5-trihydroxy-1-piperidinyl]-2,3-dioxo-1-(phenylmethyl)propyl]-, phenylmethyl ester, [2S-[1(R*),2.alpha.,3.beta.,4.alpha.,5.beta.]]- (9CI) (CA INDEX NAME)

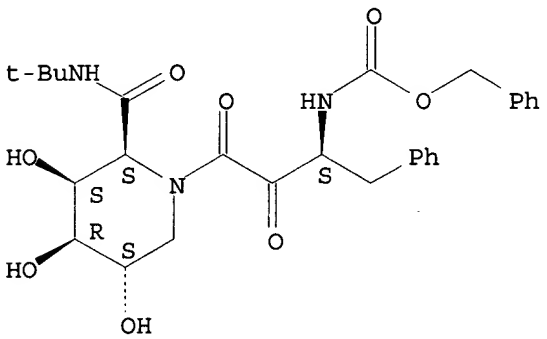
Absolute stereochemistry.





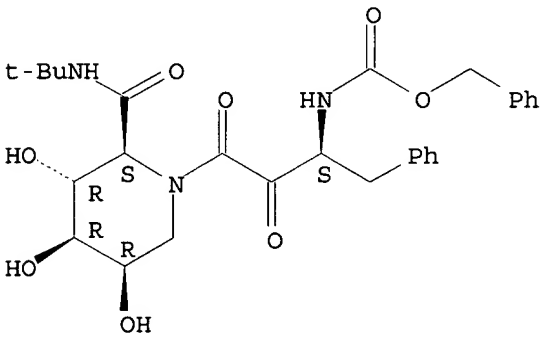
RN 191850-64-3 CAPLUS
CN Carbamic acid, [3-[2-[[(1,1-dimethylethyl)amino]carbonyl]-3,4,5-trihydroxy-1-piperidinyl]-2,3-dioxo-1-(phenylmethyl)propyl]-, phenylmethyl ester, [2S-[1(R*),2.alpha.,3.alpha.,4.alpha.,5.beta.]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



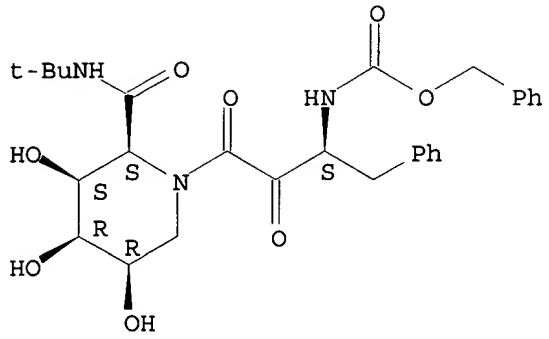
RN 191850-67-6 CAPLUS
CN Carbamic acid, [3-[2-[[(1,1-dimethylethyl)amino]carbonyl]-3,4,5-trihydroxy-1-piperidinyl]-2,3-dioxo-1-(phenylmethyl)propyl]-, phenylmethyl ester, [2S-[1(R*),2.alpha.,3.beta.,4.alpha.,5.alpha.]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

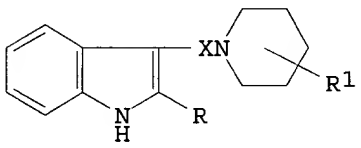


RN 191850-75-6 CAPLUS
CN Carbamic acid, [3-[2-[[(1,1-dimethylethyl)amino]carbonyl]-3,4,5-trihydroxy-1-piperidinyl]-2,3-dioxo-1-(phenylmethyl)propyl]-, phenylmethyl ester, [2S-[1(R*),2.alpha.,3.alpha.,4.alpha.,5.alpha.]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

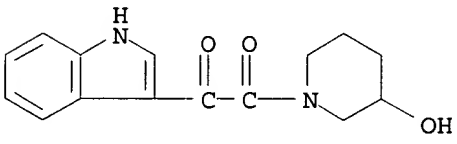


L4 ANSWER 5 OF 7 CAPLUS COPYRIGHT 2002 ACS
AN 1981:47062 CAPLUS
DN 94:47062
TI Synthesis and cardiovascular activity of piperidylethylindoles
AU Agarwal, Jagdish C.; Sharma, M.; Saxena, A. K.; Kishor, K.; Bhargava, K. P.; Shanker, K.
CS Dep. Pharmacol. Ther., King George's Med. Coll., Lucknow, India
SO Journal of the Indian Chemical Society (1980), 57(7), 742-3
CODEN: JICSAH; ISSN: 0019-4522
DT Journal
LA English
GI

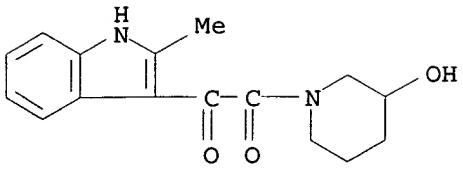


I, X=CH_2CH_2
II, X=COCO

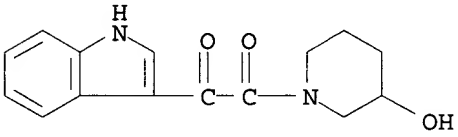
AB The piperidinoethylindoles I (R = H, Me, Ph; R1 = 2-Me, 3-Me, 4,4-Ph, HO) were prepd. by reaction of the corresponding piperidine with indoleglyoxylyl chloride to give II which were reduced with LiAlH4 to give I. Three compds. showed mild hypotensive activity and 2 compds. produced a short lasting hypertensive effect.
IT **71765-50-9P 71765-53-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and redn. of)
RN 71765-50-9 CAPLUS
CN 3-Piperidinol, 1-(1H-indol-3-yloxoacetyl)- (9CI) (CA INDEX NAME)



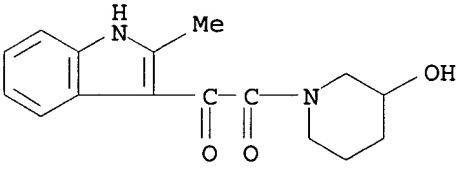
RN 71765-53-2 CAPLUS
CN 3-Piperidinol, 1-[(2-methyl-1H-indol-3-yl)oxoacetyl]- (9CI) (CA INDEX NAME)



L4 ANSWER 6 OF 7 CAPLUS COPYRIGHT 2002 ACS
AN 1979:568360 CAPLUS
DN 91:168360
TI Pharmacological evaluation of some newer piperidyl ethyl indoles as anti-parkinsonian agent
AU Agarwal, Jagdish C.; Nath, C.; Sharma, M.; Kishor, K.; Shanker, K.; Gupta, G. P.; Bhargava, K. P.
CS Dep. Pharmacol. Ther., King George's Med. Coll., Lucknow, India
SO Indian Drugs (1979), 16(9), 209-12
CODEN: INDRBA; ISSN: 0019-462X
DT Journal
LA English
AB The antiparkinsonian and analgesic activities and the effects on locomotor activities of 23 indole derivs. were studied in rats and mice, and among these, 4 compds. antagonized oxotremorine-induced tremors, 10 antagonized reserpine-induced rigidity, and 1 decreased the locomotor activity, while 2 increased it. Only 2 compds. showed mild analgesic activity.
IT **71765-50-9 71765-53-2**
RL: BIOL (Biological study)
(as antiparkinsonian drug)
RN 71765-50-9 CAPLUS
CN 3-Piperidinol, 1-(1H-indol-3-yloxoacetyl)- (9CI) (CA INDEX NAME)



RN 71765-53-2 CAPLUS
CN 3-Piperidinol, 1-[(2-methyl-1H-indol-3-yl)oxoacetyl]- (9CI) (CA INDEX NAME)

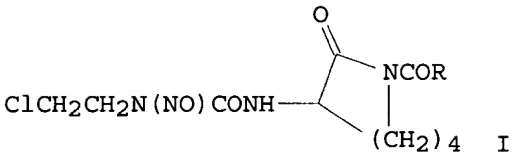


L4 ANSWER 7 OF 7 CAPLUS COPYRIGHT 2002 ACS
AN 1978:443156 CAPLUS
DN 89:43156
TI Nitrosourea derivatives
IN Matsumoto, Jun; Murakami, Masuo; Sato, Noriaki; Hashimoto, Shinichi; Kawamura, Tsutomu; Ichikawa, Kaichiro
PA Yamanouchi Pharmaceutical Co., Ltd., Japan
SO Japan. Kokai, 6 pp.
CODEN: JKXXAF

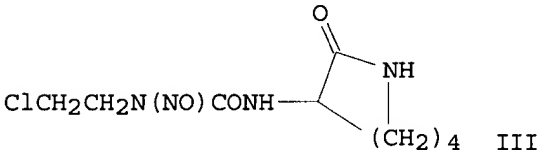
DT Patent
LA Japanese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 53034790	A2	19780331	JP 1976-109628	19760913

PI
GI



I

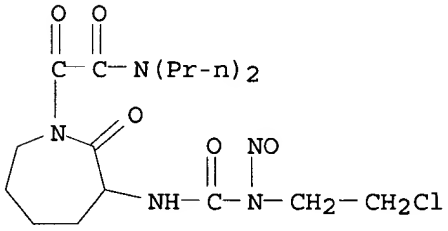


III

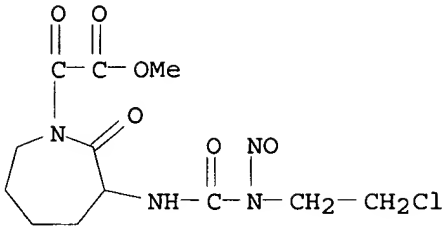
AB Nitrosourea derivs. I [R = 2-phenyl-2H-1,2,3-triazol-4-yl (II), 1-phenylpyrazol-5-yl, 4-methylphthalazan-3-yl, 1-adamantyl, 4-chloro-2-phenylpyrimidin-5-yl, Pr2NCO, 2,6-dioxopiperidin-4-ylmethyl, MeO2C] were prepd. by silylation of III followed by reaction of RCOX (X = halo). I had antileukemic and anticarcinogenic activities (no data). Thus, 1.68 mL Et3N in dioxane was added to a mixt. of 2.62 g III and 1.29 g Me3SiCl in dioxane, the whole stirred 20 h at room temp., filtered, and the filtrate concd. to give 10 mL soln.; 2-phenyl-1,2,3-triazol-4-carbonyl chloride (1.5 g) in CH2Cl2 was added to 6 mL of the soln. and the mixt. stirred 3 days at room temp. to give 165 mg II.

IT **67060-46-2P 67060-48-4P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

RN 67060-46-2 CAPLUS
CN 1H-Azepine-1-acetamide, 3-[[[(2-chloroethyl)nitrosoamino]carbonyl]amino]hexahydro-.alpha.,2-dioxo-N,N-dipropyl- (9CI) (CA INDEX NAME)



RN 67060-48-4 CAPLUS
CN 1H-Azepine-1-acetic acid, 3-[[[(2-chloroethyl)nitrosoamino]carbonyl]amino]hexahydro-.alpha.,2-dioxo-, methyl ester (9CI) (CA INDEX NAME)

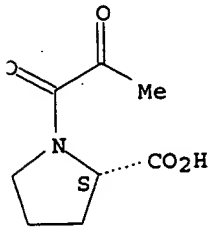


ANSWER 1 OF 16 CA COPYRIGHT 2002 ACS
123:170197 CA
Process for the stereoselective preparation of L-alanyl-L-proline via stereoselective hydrogenation/hydrogenolysis of N-(2-iminopropionyl)-L-proline
Burbaum, Beverly W.; Li, Chunshi; Matcham, George W.
Celgene Corp., USA
U.S., 6 pp. Cont.-in-part of U.S. 5,319,098.
CODEN: USXXAM
Patent
English
AN.CNT 2

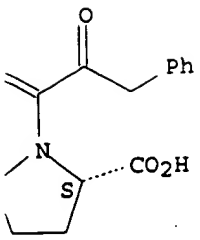
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5424454	A	19950613	US 1994-249326	19940526 <--
US 5319098	A	19940607	US 1993-63434	19930518 <--
RAI US 1993-63434		19930518		

S CASREACT 123:170197; MARPAT 123:170197
B L-Alanyl-L-proline is stereoselectively prepd. by catalytically hydrogenating an N-(2-iminopropionyl)-L-proline in the presence of a metal hydrogenolysis catalyst and at a pH of less than about 4. Also disclosed are improved processes for prodn. of N-pyruvyl-L-proline in which L-proline and a 2,2-disubstituted propionyl halide are allowed to react at a pH of at least 9 to produce an L-proline intermediate which is hydrolyzed at a pH range of from about 6.5 to about 8.5 to yield N-pyruvyl-L-proline. Thus, e.g., N-pyruvyl-L-proline [prepn. given via 2,2-dichloropropionyl chloride and N-(2,2-dichloropropionyl)proline] was treated with naphth-1-ylmethylamine for 3 h at 25.degree., and the reaction mixt. submitted to hydrogenation over Pd/C; L-alanyl-L-proline was formed in 31% d.e. (88% conversion).
IT **76391-12-3P** , N-Pyruvyl-L-proline
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 76391-12-3 CA
CN L-Proline, 1-(1,2-dioxopropyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

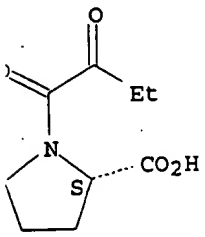


L4 ANSWER 2 OF 16 CA COPYRIGHT 2002 ACS
AN 121:212542 CA
TI 1-[4-(2-Hydroxy-3-tert-butylaminopropoxy)-indole-3-yl (5-acetamido-1-(S)-carboxypentyl)-DL-alanyl]-L-proline dihydrochloride, a new angiotensin-converting enzyme inhibitor with .beta.-adrenoblocking properties
AU Mashkovskii, M. D.; Vinogard, L. Kh.; Yuzhakov, S. D.; Dolgun, O. V.; Krit, N. A.; Filatova, M. P.; Dukhanina, Ye. A.; Dugin, S. F.; Tribunskaya, Yu. N.
CS VNIKhFI, Moscow, Russia
SO Khim.-Farm. Zh. (1993), 27(10), 16-20
CODEN: KHFZAN; ISSN: 0023-1134
DT Journal
LA Russian
GI



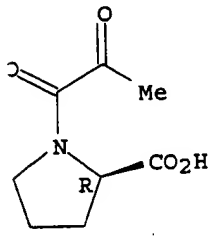
N 155404-01-6 CA
N L-Proline, 1-(1,2-dioxobutyl)- (9CI) (CA INDEX NAME)

bsolute stereochemistry.



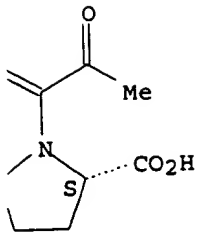
RN 155404-04-9 CA
CN D-Proline, 1-(1,2-dioxopropyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



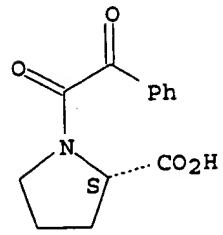
L4 ANSWER 5 OF 16 CA COPYRIGHT 2002 ACS
AN 115:248086 CA
TI Dehydrodidemnin B
IN Rinehart, Kenneth L.; Lithgow-Bertelloni, Anna M.
PA Pharma Mar S. A. (PHARMAR), Spain; Ruffles, Graham Keith
SO PCT Int. Appl., 41 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9104985	A1	19910418	WO 1990-GB1495	19901001 <--
	W: AU, JP, US				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, IT, LU, NL, SE				
	AU 9064412	A1	19910428	AU 1990-64412	19901001 <--
	AU 642169	B2	19931014		
	EP 493480	A1	19920708	EP 1990-914541	19901001 <--
	EP 493480	B1	19960117		
	R: AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, LU, NL, SE				
	JP 05502441	T2	19930428	JP 1990-513643	19901001 <--
	JP 2919965	B2	19990719		
	AT 133181	E	19960215	AT 1990-914541	19901001
	ES 2082003	T3	19960316	ES 1990-914541	19901001
	US 5834586	A	19981110	US 1994-280110	19940725
	US 6153731	A	20001128	US 1998-183024	19981030
PRAI	GB 1989-22026	A	19890929		
	WO 1990-GB1495	A	19901001		
	US 1992-844567	B1	19920424		
	US 1994-280110	A3	19940725		



L4 ANSWER 7 OF 16 CA COPYRIGHT 2002 ACS
AN 112:44174 CA
TI Stereochemistry of electrochemical reduction of optically active .alpha.-ketoamides. II. Electroreduction of benzoylformamides derived from S-(-)-proline
AU Boulmedais, Ali; Jubault, Michel; Tallec, Andre
CS Lab. Electrochim., CNRS, Rennes, 35042, Fr.
SO Bull. Soc. Chim. Fr. (1989), (2), 185-91
CODEN: BSCFAS; ISSN: 0037-8968
DT Journal
LA French
AB Electrochem. redn. of benzoylformamides derived from S-(-)-proline was carried out at a Hg cathode in a buffered hydroalcoholic medium. Quant. formation of a mixt. of the two epimers of the corresponding mandelamides is obsd. Detn. of the diastereoisomeric excess can be achieved either by proton NMR at 300 MHz or by polarimetry on the mixt. of mandelic acids formed by hydrolysis. An excess of the SS epimer is generally obtained and the optical yield can reach 50%. Influence of the electrolysis conditions (cathodic potential, compn. of the supporting electrolyte) was investigated in order to explain the obsd. results.
IT **124778-23-0**
RL: RCT (Reactant)
(redn. of, electrochem., on mercury, stereochem. in)
RN 124778-23-0 CA
CN L-Proline, 1-(oxophenylacetyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 8 OF 16 CA COPYRIGHT 2002 ACS
AN 111:195414 CA
TI Preparation of N-(carboxyalkyl)dipeptides for treatment of hypertension and congestive heart failure and pharmaceutical compositions containing them
IN Gold, Elijah H.; Neustadt, Bernard R.; Smith, Elizabeth M.
PA Schering Corp., USA
SO U.S., 8 pp. Cont.-in-part of U.S. Ser. No. 29,293.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 6

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 4818749	A	19890404	US 1987-117008	19871104 <--
	EP 50800	A1	19820505	EP 1981-108348	19811015 <--
	EP 50800	B1	19860618		
	EP 50800	B2	19950607		
	R: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
	ZA 8107261	A	19820929	ZA 1981-7261	19811020 <--
	US 4808573	A	19890228	US 1987-29293	19870323 <--

US 1981-295137 19810821

B Title compds. (R)xCR1R2X(CH2)mCR3R7CONR4CR5(R8)yCOR6 [R = H, (un)substituted Me, allyl, Me2CHCH2, Et, mercaptoalkyl, hydroxyalkyl, BzNH, AcNH, etc., R1 and R3 = a wide range of claimed groups; R2 = CO2R9, CH2CO2R9, COSR9, CH2COSR9, CH2SR9 [R9 = H, Ph, CH2Ph, C1-5 alkyl, CONR10R11 (R10, R11 = H, Ph, CH2Ph, C1-5 alkyl)]; R4 and R5 form heterocyclic ring; R6 = NH2, OR12, SR12 (R12 = H, C1-3 alkyl); R7 = H, Me, halomethyl, CH2OH, CH2NH2, CH2SH; R8 = H, Me, F, Cl, Br; X = S, O, NH, NMe; x and y = 0 or 1; m = 0, 1] were prepd. as angiotensin-converting enzyme (ACE) inhibitors and antihypertensives. Thus, D-HSCH2CHMeCO-L-Pro-OH was treated with MeCHBrCO2H in aq. EtOH contg. K2CO3 to give D-HO2CCHMeSCH2CHMeCO-L-Pro-OH, which at 1.5 .times. 10-6 M inhibited ACE by 50%.

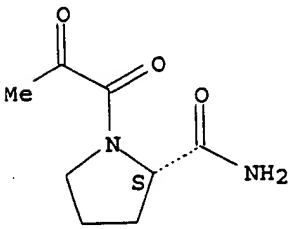
06.7.8

IT 83080-42-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and reaction of, with phenylalanine)

RN 83080-42-6 CA

CN 2-Pyrrolidinecarboxamide, 1-(1,2-dioxopropyl)-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

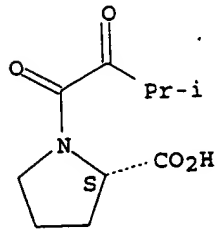


IT 83079-95-2P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

RN 83079-95-2 CA

CN L-Proline, 1-(3-methyl-1,2-dioxobutyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

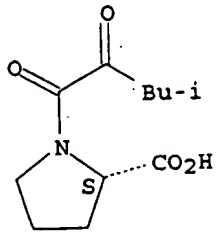


IT 83079-96-3
RL: RCT (Reactant)
(reaction of, with glutamic acid deriv.)

RN 83079-96-3 CA

CN L-Proline, 1-(4-methyl-1,2-dioxopentyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 76391-12-3
RL: RCT (Reactant)
(reaction of, with homocysteine ketone deriv.)

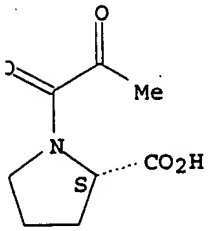
	JP 04080009	B4	19921217	
	JP 02131496	A2	19900521	JP 1989-238330 19890913 <--
	JP 04042400	B4	19920713	
PRAI	US 1978-968249		19781211	
	CA 1979-341340		19791206	
	EP 1979-105015		19791210	
	CS 1979-8645		19791211	

AB Antihypertensive RCOCR1R2NHCHR3COR4CR5R6COR7 (I, R, R7 = optionally substituted alkoxy, aryloxy, alkenoxy, NH2, alkylamino, HONH; R1-R6 = H, optionally substituted alkyl, Ph; R4R5 = alkylene) were prepd. Thus, H-Ala-Pro-OH was treated with Me2CH(CH2)3COCO2H in the presence of NaCNBH3 to give Me2CH(CH2)3CH(CO2H)-Ala-Pro-OH which was characterized by its spectra.

IT **76391-12-3**
RL: RCT (Reactant)
(peptide coupling of)

RN 76391-12-3 CA
CN L-Proline, 1-(1,2-dioxopropyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

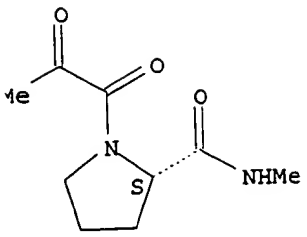


L4 ANSWER 16 OF 16 CA COPYRIGHT 2002 ACS
AN 81:169816 CA
TI Amino acids and peptides. XI. Synthesis attempts in the series of the 3,6-epidithio-2,5-dioxopiperazine antibiotics gliotoxin, sporidesmin, aranotin, chaetocin, and verticillin. VIII. Hydroxycyclodipeptides by cyclization of pyruvyl amino acids
AU Haeusler, Johannes; Schmidt, Ulrich
CS Org.-Chem. Inst., Univ. Wien, Vienna, Austria
SO Chem. Ber. (1974), 107(9), 2804-15
CODEN: CHBEAM
DT Journal
LA German
GI For diagram(s), see printed CA Issue.
AB Pyruvoyl amino acid amides are synthesized by means of activated pyruvic acid compds. (pyruvoyl chloride, p-nitrophenyl pyruvate, and hydroxymaleic anhydride). These undergo ring closure (optimally in H2O at pH 7.5) to yield the hydroxycyclodipeptides I-V. The equil. lies completely on the side of the cyclic compd. regardless of the structure of the pyruvic acid compd. In the case of the proline deriv. VI, cyclization occurs with high optical induction to yield the kinetically controlled isomer I, which rearranges in acidic and basic aq. soln. with high optical induction to the thermodynamically stable isomer II. Under specific mercaptalizing reaction conditions, the OH group can be replaced by S groups, usually with high optical induction.

IT **53935-74-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and ring closure of)

RN 53935-74-3 CA
CN 2-Pyrrolidinecarboxamide, 1-(1,2-dioxopropyl)-N-methyl-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

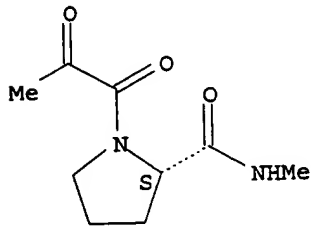


IT 53935-75-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 53935-75-4 CA X
CN 2-Pyrrolidinecarboxamide, 1-(1,2-dioxopropyl)-N-methyl-, mono[(2,4-dinitrophenyl)hydrazone], (S)- (9CI) (CA INDEX NAME)

CM 1

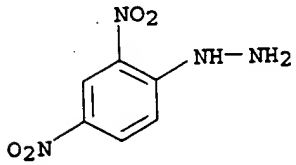
CRN 53935-74-3
CMF C9 H14 N2 O3
CDES 1:S

Absolute stereochemistry.



CM 2

CRN 119-26-6
CMF C6 H6 N4 O4



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FULL ESTIMATED COST	73.93	214.98
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-10.03	-10.03

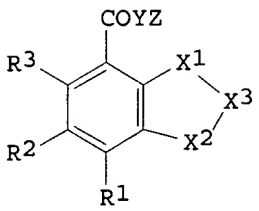
STN INTERNATIONAL LOGOFF AT 20:51:21 ON 07 APR 2002

Host Name: +++
OK
ATHZ
OK

AN 1993:539245 CAPLUS
DN 119:139245
TI Preparation of 1,4-benzodioxan-5-carboxylates and analogs as 5-HT4 receptor antagonists
IN King, Francis David; Gaster, Laramie Mary; Mulholland, Keith Raymond; Rahman, Shirley Katherine; Wyman, Paul Adrian; Sanger, Gareth John; Wardle, Kay Alison; Baxter, Gordon Smith; Kennett, Guy Anthony; Kaumann, Alberto Julio
PA SmithKline Beecham PLC, UK
SO PCT Int. Appl., 55 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 9

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9305038	A1	19930318	WO 1992-GB1649	19920909
	W: AT, AU, BB, BG, BR, CA, CH, CS, DE, DK, ES, FI, GB, HU, JP, KP, KR, LK, LU, MG, MN, MW, NL, NO, PL, RO, RU, SD, SE, US				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, SE				
	AU 9225418	A1	19930405	AU 1992-25418	19920909
	AU 668102	B2	19960426		
	EP 604494	A1	19940706	EP 1992-919260	19920909
	EP 604494	B1	19990728		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, SE				
	BR 9206599	A	19941108	BR 1992-6599	19920909
	JP 06510537	T2	19941124	JP 1992-505071	19920909
	HU 70154	A2	19950928	HU 1994-734	19920909
	CZ 283619	B6	19980513	CZ 1994-560	19920909
	RU 2124512	C1	19990110	RU 1994-17664	19920909
	AT 182591	E	19990815	AT 1992-919260	19920909
	ES 2135414	T3	19991101	ES 1992-919260	19920909
	JP 3294611	B2	20020624	JP 1993-505071	19920909
	ZA 9206889	A	19930524	ZA 1992-6889	19920910
	ZA 9206890	A	19930614	ZA 1992-6890	19920910
	CN 1073173	A	19930616	CN 1992-110597	19920910
	CN 1040436	B	19981028		
	IL 103138	A1	19990509	IL 1992-103138	19920911
	ES 2065238	B1	19951001	ES 1992-2353	19921120
	ES 2065238	A1	19950201		
	ZA 9300764	A	19931126	ZA 1993-764	19930204
	FI 9401178	A	19940311	FI 1994-1178	19940311
	NO 9400874	A	19940311	NO 1994-874	19940311
	US 5580885	A	19961203	US 1994-204429	19940728
	AU 9660735	A1	19961003	AU 1996-60735	19960726
	AU 691430	B2	19980514		
PRAI	GB 1991-19449	A	19910912		
	GB 1991-19692	A	19910914		
	GB 1991-22473	A	19911023		
	GB 1991-22474	A	19911023		
	GB 1991-22624	A	19911024		
	GB 1992-1413	A	19920123		
	GB 1992-1414	A	19920123		
	GB 1992-2510	A	19920206		
	GB 1992-14399	A	19920707		
	WO 1992-GB1649	A	19920909		

OS MARPAT 119:139245
GI



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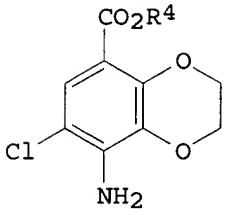


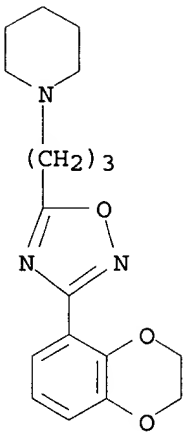
II

AB Title compds. [I; R3 = H, NH2, halo, alkyl, alkoxy; R1 = groups cited for R3, OH; R2 = groups cited for R3, NO2, alkylthio; X1 = O, S; X2 = O, S, NR, NRCO; R = H, alkyl; X3 = (alkyl substituted) (CH2)1-3; Y = O, NH; Z = aminoalkyl, satd. N-contg. heterocyclylalkyl; COY may be replaced by a heterocyclic **bioisostere**] were prepd. Thus, title compd. II (R4 = H) was esterified by 1-butyl-4-piperidinemethanol (prepn. given) to give II (R4 = 1-butyl-4-piperidylmethyl) which increased social interaction in rats at 0.001-1.0 mg/kg s.c.

IT **148688-09-9P 148702-74-3P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as serotoninergic antagonist)

RN 148688-09-9 CAPLUS

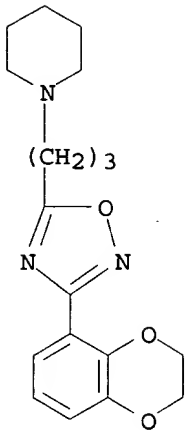
CN Piperidine, 1-[3-[3-(2,3-dihydro-1,4-benzodioxin-5-yl)-1,2,4-oxadiazol-5-yl]propyl]-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

RN 148702-74-3 CAPLUS

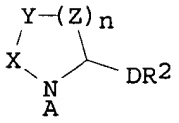
CN Piperidine, 1-[3-[3-(2,3-dihydro-1,4-benzodioxin-5-yl)-1,2,4-oxadiazol-5-yl]propyl]- (9CI) (CA INDEX NAME)


N
(CH2)3
O
N
N
O
O

AN 2000:133477 CAPLUS
DN 132:175848
TI Carboxylic acids and isosteres of heterocyclic ring compounds having multiple heteroatoms for vision and memory disorders
IN Ross, Douglas T.; Sauer, Hansjorg; **Hamilton, Gregory S.**; Steiner, Joseph P.
PA Guilford Pharmaceuticals Inc., USA
SO PCT Int. Appl., 91 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000009106	A2	20000224	WO 1999-US18238	19990812
	WO 2000009106	A3	20001012		
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	US 6337340	B1	20020108	US 1998-134476	19980814
	CA 2336154	AA	20000224	CA 1999-2336154	19990812
	AU 9953970	A1	20000306	AU 1999-53970	19990812
	EP 1104300	A2	20010606	EP 1999-939731	19990812
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	JP 2002522482	T2	20020723	JP 2000-564609	19990812
PRAI	US 1998-134476	A	19980814		
	WO 1999-US18238	W	19990812		

OS MARPAT 132:175848
GI



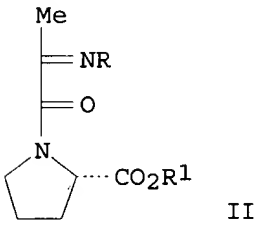
I

AB The title compds. [I; X, Y, Z = C, O, S, N; A = R1C(O)C(O), R1C(O)C(S), R1SO2, R1(E)NC(O); R1, E = H, C1-9 alkyl, C2-9 alkenyl, aryl, heteroaryl, carbocyclyl, heterocyclyl; D = bond, (substituted) C1-10 alkylene, CH:CH; R2 = CO2H, carboxylic acid isostere; n = 1-3] are prepd. for treating vision disorders, improving vision, treating memory impairment, or enhancing memory performance in an animal. I bind to immunophilin FKBP12 and preferably do not have immunosuppressive activity. Affinity for FKBP12 is measured as inhibition of prolyl peptidyl cis-trans isomerase (rotamase). Thus, GPI 1046 (10 mg/kg s.c.) protected retinal ganglion cells and optic nerve axons and myelin against degeneration following retinal ischemia in rats, and protected against retinal ganglion cell death after optic nerve transection. Me 1,3-**oxazolidine**-4-carboxylate was condensed with Me oxalyl chloride and the product reacted with 1,1-dimethylpropylmagnesium chloride and sapon. to produce 3-(3,3-dimethyl-2-oxopentanoyl)-1,3-**oxazolidine**-4-carboxylic acid, I [X = Z = CH2, Y = O, A = CH3CH2CMe2C(O)C(O), D = bond, R2 = CO2H, n = 1].

AN 1994:509686 CAPLUS
DN 121:109686
TI stereoselective preparation of alanylproline via hydrogenation of iminopropionylproline.
IN Burbaum, Beverly W.; Li, Chunshi; Matcham, George W.
PA Celgene Corp., USA
SO U.S., 5 pp.
CODEN: USXXAM
DT **Patent**
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5319098	A	19940607	US 1993-63434	19930518 <--
	WO 9426771	A1	19941124	WO 1994-US5553	19940518 <--
	W: CA, JP				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	US 5424454	A	19950613	US 1994-249326	19940526 <--
PRAI	US 1993-63434		19930518		

OS CASREACT 121:109686; MARPAT 121:109686
GI



II

AB Alanylproline (I) is stereoselectively prepd. catalytically hydrogenating N-(2-iminopropionyl)-L-**proline** (II; R = hydrogenolytically labile group; R1 = H, hydrogenolytically removable protecting group) in the presence of a metal hydrogenolysis catalyst and at a pH of less than about 4. Thus, N-**pyruvylproline** (prepn. from **proline** and a 2,2-disubstituted propionyl halide given) was refluxed 2 h with NH2OH.HCl and NaOAc in EtOH/H2O for 2 h; the mixt. was dild. with EtOH and palladium hydroxide on C and HCl were added followed by hydrogenation for 17 h at 50 psi to give I of >99.5% diastereomeric purity.

AN 1998:503787 CAPLUS
DN 129:226091
TI TGF-.beta.-signaling with small molecule FKBP12 antagonists that bind myristoylated FKBP12-TGF-.beta. type I receptor fusion proteins
AU Stockwell, Brent R.; Schreiber, Stuart L.
CS Howard Hughes Medical Inst., Dep. Chem. Chem. Biol., Harvard Univ., Cambridge, MA, 02138, USA
SO Chemistry & Biology (1998), 5(7), 385-395
CODEN: CBOLE2; ISSN: 1074-5521
PB Current Biology Ltd.
DT Journal
LA English
RE.CNT 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

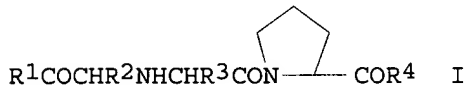
AB Growth arrest in many cell types is triggered by transforming growth factor beta (TGF-.beta.), which signals through two TGF-.beta. receptors (type I, TGF-.beta.RI, and type II, TGF-.beta.RII). In the signaling pathway, TGF-.beta. binds to the extracellular domain of TGF-.beta.RII, which can then transphosphorylate TGF-.beta.RI in its glycine/serine (GS)-rich box. Activated TGF-.beta.RI phosphorylates two downstream effectors, Smad2 and Smad3, leading to their translocation into the nucleus. Cell growth is arrested and plasminogen activator inhibitor 1 (PAI-1) is upregulated. The authors investigated the role of the **immunophilin** FKBP12, which can bind to the GS box of TGF-.beta.RI, in TGF-.beta. signaling. Overexpression of myristoylated TGF-.beta.RI and TGF-.beta.RII cytoplasmic tails caused constitutive nuclear translocation of a green-fluorescent-protein-Smad2 construct in COS-1 cells, and constitutive activation of a PAI-1 reporter plasmid in mink lung cells. Fusing FKBP12 to TGF-.beta.RI resulted in repression of autosignaling that could be alleviated by FK506M or rapamycin (two small mols. that can bind to FKBP12). Mutation of the FKBP12-binding site in the FKBP12-TGF-.beta.RI fusion protein restored constitutive signaling. An **acidic** mutation in the FKBP12-TGF.beta.RI protein allowed FKBP12 antagonists to activate signaling in the absence of TGF-.beta.RII. Further mutations in the TGF-.beta.RI FKBP12-binding site resulted in TGF-.beta. signaling that was independent of both TGF-.beta.RII and FKBP12 antagonists. Fusing FKBP12 to TGF-.beta.RI results in a novel receptor that is activated by small mol. FKBP12 antagonists. These results suggest that FKBP12 binding to TGF-.beta.RI is inhibitory and that FKBP12 plays a role in inhibiting TGF-.beta. superfamily signals.

IT Protein motifs
(leucine-**proline**; TGF-.beta.-signaling with small mol. FKBP12 antagonists that bind myristoylated FKBP12-TGF-.beta. type I receptor fusion proteins)

AN 1989:497735 CAPLUS
DN 111:97735
TI Preparation of proline- and perhydroindolecarboxylate-containing dipeptides as antihypertensives
IN Gold, Elijah H.; Neustadt, Bernard R.; Smith, Elizabeth M.
PA Schering Corp., USA
SO U.S., 6 pp. Cont.-in-part of U.S. Ser. No. 258,484, abandoned.
CODEN: USXXAM
DT **Patent**
LA English
FAN.CNT 6

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 4808573	A	19890228	US 1987-29293	19870323 <--
	EP 50800	A1	19820505	EP 1981-108348	19811015 <--
	EP 50800	B1	19860618		
	EP 50800	B2	19950607		
	R: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
	ZA 8107261	A	19820929	ZA 1981-7261	19811020 <--
	US 4818749	A	19890404	US 1987-117008	19871104 <--
PRAI	US 1980-199886		19801023		
	US 1980-201649		19801028		
	US 1981-258484		19810428		
	EP 1981-108348		19811015		
	US 1981-334053		19811223		
	US 1987-29293		19870323		

OS MARPAT 111:97735
GI



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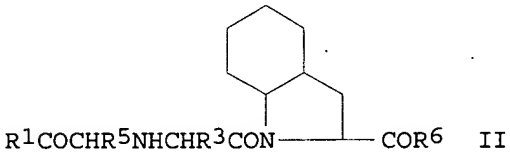

II

AB The title compds. [I and II; R1,R4 = OH, alkoxy; R2 = PhCH2SCH2, PhCH2CH2SCH2, naphthylmethylthiomethyl, methylbenzylthiomethyl, 2-(carboxyphenyl)ethyl, 2-(alkoxycarbonylphenyl)ethyl; R3 = H, alkyl, aminoalkyl; R5 = benzyloxyalkyl, benzylthioalkyl], useful as angiotencin converting enzyme (ACE) inhibitors (no data), were prepd. A mixt. of S-benzyl-L-cysteine Et ester, N-**pyruvoyl**-L-**proline**, and 5.ANG. sieves was stirred 2 days in THF. NaBH3CN in EtOH was added and the mixt. was stirred 18 h to give N-[(1R)-ethoxycarbonyl-2-benzylthioethyl]-(R,S)-alanyl-(S)-**proline**-HCl.

L3 ANSWER 7 OF 9 CAPLUS COPYRIGHT 2002 ACS
AN 1989:189731 CAPLUS
DN 110:189731
TI Tissue-culture method for selection and production of herbicide-resistant plants
IN Donn, Guenter
PA Hoechst A.-G., Fed. Rep. Ger.
SO Eur. Pat. Appl., 11 pp.
CODEN: EPXXDW
DT **Patent**

LA German
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	EP 290987	A2	19881117	EP 1988-107373	19880507	<--
	EP 290987	A3	19910904			
	EP 290987	B1	19941123			
	R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE					
	DE 3715958	A1	19881124	DE 1987-3715958	19870513	<--
	ES 2066769	T3	19950316	ES 1988-107373	19880507	<--
	FI 8802203	A	19881114	FI 1988-2203	19880511	<--
	ZA 8803345	A	19881228	ZA 1988-3345	19880511	<--
	HU 49977	A2	19891228	HU 1988-2369	19880511	<--
	AU 8816095	A1	19881117	AU 1988-16095	19880512	<--
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	CA 1310928	A1	19921201	CA 1988-566573	19880512	<--
	CN 1026205	B	19941019	CN 1988-102755	19880512	<--
	IL 86358	A1	19941229	IL 1988-86358	19880512	<--
PRAI	DE 1987-3715958		19870513			

OS MARPAT 110:189731

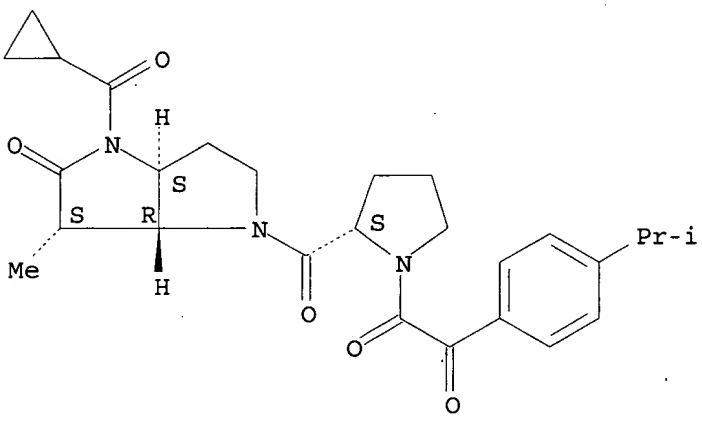
AB Herbicide-resistant plant cell lines are produced by selecting callus cultures or cell suspensions which can grow in amino acid-free media and retain their ability to regenerate whole plants, and growing these in amino acid-free media contg. amino acid biosynthesis inhibitors, to select for inhibitor-resistant cultures. Herbicide-resistant plants are regenerated from these cultures. Corn embryonic tissue was cultured in callus induction medium (e.g. modified MS-medium contg. **proline**, asparagine, glutamine, casein hydrolyzate, and sucrose), and the calli so obtained were then cultured in amino acid-free modified MS-medium contg. citric acid, .alpha.-ketoglutarate, malic acid, oxaloacetate, succinic acid, and **pyruvic** acid. Tissue from the resulting calli was mutagenized with ethyl methanesulfonate, and calli were regenerated from the surviving tissue. These mutant calli were cultured in media contg. herbicide at a concn. sufficient to kill 95-99% of the calli, e.g. 0.2 mM glufosinate, and the herbicide-resistant plants were regenerated from the surviving calli.

AN 1997:412743 CAPLUS
DN 127:132694
TI Structural and functional analysis of the mitotic rotamase Pin1 suggests substrate recognition is phosphorylation dependent
AU Ranganathan, Rama; Lu, Kun Ping; Hunter, Tony; Noel, Joseph P.
CS Structural Biology Laboratory, The Salk Institute for Biological Studies, La Jolla, CA, 92037, USA
SO Cell (Cambridge, Massachusetts) (1997), 89(6), 875-886
CODEN: CELLB5; ISSN: 0092-8674
PB Cell Press
DT Journal
LA English
AB The human **rotamase** or peptidyl-prolyl cis-trans isomerase Pin1 is a conserved mitotic regulator essential for the G2/M transition of the eukaryotic cell cycle. We report the 1.35 .ANG. crystal structure of Pin1 complexed with an AlaPro dipeptide and the initial characterization of Pin1's functional properties. The crystallog. structure as well as pH titrn. studies and mutagenesis of an active site cysteine suggest a catalytic mechanism that includes general acid-base and covalent catalysis during peptide bond isomerization. Pin1 displays a preference for an acidic residue N-**terminal** to the isomerized **proline** bond due to interaction of this acidic side chain with a basic cluster. This raises the possibility of phosphorylation-mediated control of Pin1-substrate interactions in cell cycle regulation.

IN Pyrrolo[3,2-b]pyrrol-2(1H)-one, 1-(cyclopropylcarbonyl)hexahydro-3-methyl-4-[[(2S)-1-[[4-(1-methylethyl)phenyl]oxoacetyl]-2-pyrrolidinyl]carbonyl]-, (3S,3aR,6aS)- (9CI)

MF C27 H33 N3 O5

Absolute stereochemistry.



AN 2001:916406 CAPLUS
DN 136:31715
TI Carboxylic acids and carboxylic acid isosteres of N-heterocyclic compounds, preparation thereof, and use in the treatment of neurological and other disorders
IN Hamilton, Gregory S.; Norman, Mark H.; Wu, Yong-Qian
PA GPI Nil Holdings, Inc., USA
SO U.S., 62 pp., Cont.-in-part of U.S. Ser. No. 204,237, abandoned.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 5

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6331537	B1	20011218	US 1999-453571	19991202
	ZA 9811063	A	20000707	ZA 1998-11063	19981203
	WO 2000032588	A2	20000608	WO 1999-US28663	19991203
	WO 2000032588	A3	20010222		
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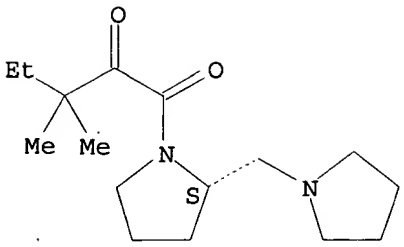
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	BR 9916461	A	20010904	BR 1999-16461	19991203
	EP 1135370	A2	20010926	EP 1999-961930	19991203
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	NO 2001002765	A	20010720	NO 2001-2765	20010605
	BG 105643	A	20020228	BG 2001-105643	20010625
PRAI	US 1998-87788P	P	19980603		
	US 1998-204237	B2	19981203		
	US 1999-453571	A	19991202		
	WO 1999-US28663	W	19991203		

OS MARPAT 136:31715
AB N-heterocyclic carboxylic acids and carboxylic acid isosteres are provided, as are their prepn. and their use for treating neurol. disorders including phys. damaged nerves and neurodegenerative diseases, for treating alopecia and promoting hair growth, for treating vision disorders and/or improving vision, and for treating memory impairment and/or enhancing memory performance by administering such compds.
IT **273924-87-1P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(carboxylic acids and carboxylic acid isosteres of N-heterocyclic compds., prepn., and use in treatment of neurol. and other disorders)
RN 273924-87-1 CAPLUS
CN Pyrrolidine, 1-(3,3-dimethyl-1,2-dioxopentyl)-2-(1-pyrrolidinylmethyl)-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 364 THERE ARE 364 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

AN 2000:384175 CAPLUS
DN 133:30959
TI Preparation of prolinylalkanediones and related compounds for treating neurological disease, vision disorders, and alopecia.
IN Hamilton, Gregory S.; Norman, Mark H.; Wu, Yong-qian
PA GPI Nil Holdings, Inc., USA; Amgen, Inc.
SO PCT Int. Appl., 166 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 5

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000032588	A2	20000608	WO 1999-US28663	19991203
	WO 2000032588	A3	20010222		
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	US 6331537	B1	20011218	US 1999-453571	19991202
	BR 9916461	A	20010904	BR 1999-16461	19991203
	EP 1135370	A2	20010926	EP 1999-961930	19991203
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	NO 2001002765	A	20010720	NO 2001-2765	20010605
	BG 105643	A	20020228	BG 2001-105643	20010625
PRAI	US 1998-204237	A	19981203		
	US 1999-453571	A	19991202		
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OS MARPAT 133:30959
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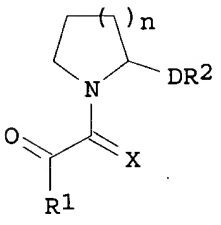


I

AB Title compds. [I; n = 1-3; X = O, S; R1 = (substituted) alkyl, alkenyl, aryl, heteroaryl, carbocyclyl, heterocyclyl; D = bond, (substituted) alkyl, alkenyl, alkynyl; R2 = CO2H, (substituted) CO2H isostere], were prepd. Thus, L-proline Me ester hydrochloride in CH2Cl2 was treated with Et3N and then with MeO2CCOCl to give 88% Me (2S)-1-(1,2-dioxo-2-methoxyethyl)-2-pyrrolidinecarboxylate. The latter in THF at -78.degree. was treated with 1,1-dimethylpropylmagnesium chloride followed by 3 h stirring at -78.degree. to give 75% Me (2S)-1-(1,2-dioxo-3,3-dimethylpentyl)-2-pyrrolidinecarboxylate. This was stirred overnight with aq. LiOH in MeOH to give 87% (2S)-1-(1,2-dioxo-3,3-dimethylpentyl)-2-

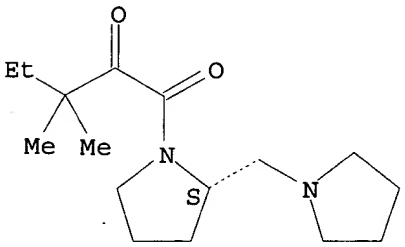
pyrrolidinecarboxylic acid. In the MPTP model of Parkinson's disease in mice, I at 10 mg/kg orally gave 10.4-46.5% recovery of TH-stained dopaminergic neurons.

IT **273924-87-1P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of prolinylalkanediones and related compds. for treating neurol. disease, vision disorders, and alopecia)

RN 273924-87-1 CAPLUS

CN Pyrrolidine, 1-(3,3-dimethyl-1,2-dioxopentyl)-2-(1-pyrrolidinylmethyl)-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



AN 1994:673586 CAPLUS
DN 121:273586
TI A novel FK506- and rapamycin-binding protein (FPR3 gene product) in the yeast Saccharomyces cerevisiae is a proline **rotamase** localized to the nucleolus
AU Benton, Bret M.; Zang, Ji-Hong; Thorner, Jeremy
CS Dep. Molecular Cell Biology, Univ. California, Berkeley, CA, 94720-3202, USA
SO Journal of Cell Biology (1994), 127(3), 623-39
CODEN: JCLBA3; ISSN: 0021-9525
DT Journal
LA English
AB The gene (FPR3) encoding a novel type of peptidylprolyl-cis-trans-isomerase (PPIase) was isolated during a search for previously unidentified nuclear proteins in Saccharomyces cerevisiae. PPIases are thought to act in conjunction with protein chaperones because they accelerate the rate of conformational interconversions around proline residues in polypeptides. The FPR3 gene product (Fpr3) is 413 amino acids long. The 111 COOH-terminal residues of Fpr3 share greater than 40% amino acid identity with a particular class of PPIases, termed FK506-binding proteins (FKBPs) because they are the intracellular receptors for two immunosuppressive compds., rapamycin and FK506. When expressed in and purified from Escherichia coli, both full-length Fpr3 and its isolated COOH-terminal domain exhibit readily detectable PPIase activity. Both fpr3.DELTA. null mutants and cells expressing FPR3 from its own promoter on a multicopy plasmid have no discernible growth phenotype and do not display any alteration in sensitivity to the growth-inhibitory effects of either FK506 or rapamycin. In S. cerevisiae, the gene for a 112-residue cytosolic FKBP (FPR1) and the gene for a 135-residue ER-assocd. FKBP (FPR2) have been described before. Even fpr1 fpr2 fpr3 triple mutants are viable. However, in cells carrying an fpr1.DELTA. mutation (which confers resistance to rapamycin), overexpression from the GAL1 promoter of the C-terminal domain of Fpr3, but not full-length Fpr3, restored sensitivity to rapamycin. Conversely, overprodn. from the GAL1 promoter of full-length Fpr3, but not its COOH-terminal domain, is growth inhibitory in both normal cells and fpr1.DELTA. mutants. In fpr1.DELTA. cells, the toxic effect of Fpr3 overprodn. can be reversed by rapamycin. Overprodn. of the NH2-terminal domain of Fpr3 is also growth inhibitory in normal cells and fpr1.DELTA. mutants, but this toxicity is not ameliorated in fpr1.DELTA. cells by rapamycin. The NH2-terminal domain of Fpr3 contains long stretches of **acidic** residues alternating with blocks of basic residues, a structure that resembles sequences found in nucleolar proteins, including S. cerevisiae NSR1 and mammalian nucleolin. Indirect immunofluorescence with polyclonal antibodies raised against either the NH2- or the COOH-terminal segments of Fpr3 expressed in E. coli demonstrated that Fpr3 is located exclusively in the nucleolus.

AN 1995:183595 CAPLUS
DN 122:26154
TI FKBP46, a novel Sf9 insect cell nuclear immunophilin that forms a protein-kinase complex
AU Alnemri, Emad S.; Fernandes-Alnemri, Teresa; Pomerenke, Klaudia; Robertson, Noreen M.; Dudley, Keith; DuBois, Garrett C.; Litwack, Gerald
CS Dep. Pharmacol. Microbiol. Immunol., The Jefferson Cancer Instit., Thomas Jefferson Univ., Philadelphia, PA, 19107, USA
SO Journal of Biological Chemistry (1994), 269(49), 30828-34
CODEN: JBCHA3; ISSN: 0021-9258
PB American Society for Biochemistry and Molecular Biology
DT Journal
LA English
AB Recently, we identified a 59-kDa nuclear phosphoprotein that is assocd. with a recombinant mouse FKBP-52 (Alnemri, E. S., Fernandes-Alemri, T., Nelki, D. S., Dudley, K., DuBois, G. C., and Litwack, G. (1993) Proc. Natl. Acad. Sci. U.S.A. 90, 6839-6843). Here we describe the cloning, overexpression, and characterization of this protein from Spodoptera frugiperda insect cells (Sf9 cells). The cloned cDNA codes for an **acidic** protein of 412 amino acids with distinct structural domains. Starting with the N terminus, the first 218 amino acids contain two highly **acidic** domains sepd. by a short basic domain. Following the second large **acidic** domain is another basic domain of 87 amino acids with significant sequence and structural homol. to HMG1 and HMG2 DNA binding proteins. The two basic domains contain several nuclear targeting signals. The last 108 C-terminal amino acids contain a binding domain for immunosuppressive drugs FK506 and rapamycin, which makes this protein a new member of the immunophilin family. We provide evidence that the new immunophilin (FKBP46) is a DNA binding protein that can bind immunosuppressive drug FK506 and possesses peptidylprolyl isomerase activity. FKBP46 is localized in the nucleus and is assocd. with a nuclear kinase that specifically phosphorylates it in the presence of Mg2+ and ATP. Upon subsequent sequence anal. of the mouse FKBP52 CDNA used in our previous study, it was obsd. that a spermatid nuclear transition protein 2 (TP2) sequence is fused in frame with the C terminus of the recombinant FKBP52 probably as a result of a cloning artifact. We demonstrate that the FKBP46 does not form a complex with the FKBP52 but rather with the highly basic nuclear protein TP2. Our data suggest that interaction of FKBP46 with TP2 is mediated by the N-terminal **acidic** domain of FKBP46. This implies that the **acidic** domain of FKBP46 is involved in protein-protein interaction between nuclear FKBP46 and other basic chromatin proteins.
AB Recently, we identified a 59-kDa nuclear phosphoprotein that is assocd. with a recombinant mouse FKBP-52 (Alnemri, E. S., Fernandes-Alemri, T., Nelki, D. S., Dudley, K., DuBois, G. C., and Litwack, G. (1993) Proc. Natl. Acad. Sci. U.S.A. 90, 6839-6843). Here we describe the cloning, overexpression, and characterization of this protein from Spodoptera frugiperda insect cells (Sf9 cells). The cloned cDNA codes for an **acidic** protein of 412 amino acids with distinct structural domains. Starting with the N terminus, the first 218 amino acids contain two highly **acidic** domains sepd. by a short basic domain. Following the second large **acidic** domain is another basic domain of 87 amino acids with significant sequence and structural homol. to HMG1 and HMG2 DNA binding proteins. The two basic domains contain several nuclear targeting signals. The last 108 C-terminal amino acids contain a binding domain for immunosuppressive drugs FK506 and rapamycin, which makes this protein a new member of the immunophilin family. We provide evidence that the new immunophilin (FKBP46) is a DNA binding protein that can bind immunosuppressive drug FK506 and possesses peptidylprolyl isomerase activity. FKBP46 is localized in the nucleus and is assocd. with a nuclear kinase that specifically phosphorylates it in the presence of Mg2+ and ATP. Upon subsequent sequence anal. of the mouse FKBP52 CDNA

used in our previous study, it was obsd. that a spermatid nuclear transition protein 2 (TP2) sequence is fused in frame with the C terminus of the recombinant FKBP52 probably as a result of a cloning artifact. We demonstrate that the FKBP46 does not form a complex with the FKBP52 but rather with the highly basic nuclear protein TP2. Our data suggest that interaction of FKBP46 with TP2 is mediated by the N-terminal **acidic** domain of FKBP46. This implies that the **acidic** domain of FKBP46 is involved in protein-protein interaction between nuclear FKBP46 and other basic chromatin proteins.

AN 2000:384175 CAPLUS
DN 133:30959
TI Preparation of prolinylalkanediones and related compounds for treating neurological disease, vision disorders, and alopecia.
IN Hamilton, Gregory S.; Norman, Mark H.; Wu, Yong-qian
PA GPI Nil Holdings, Inc., USA; Amgen, Inc.
SO PCT Int. Appl., 166 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 5

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000032588	A2	20000608	WO 1999-US28663	19991203
	WO 2000032588	A3	20010222		
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	BR 9916461	A	20010904	BR 1999-16461	19991203
	EP 1135370	A2	20010926	EP 1999-961930	19991203
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	NO 2001002765	A	20010720	NO 2001-2765	20010605
PRAI	US 1998-204237	A	19981203		
	US 1999-453571	A	19991202		
	US 1998-87788P	P	19980603		
	WO 1999-US28663	W	19991203		

OS MARPAT 133:30959
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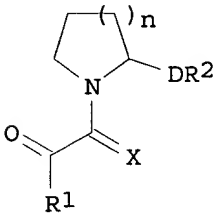


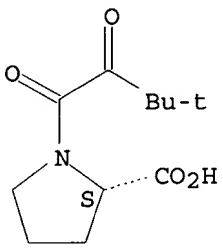
I

AB Title compds. [I; n = 1-3; X = O, S; R1 = (substituted) alkyl, alkenyl, aryl, heteroaryl, carbocyclyl, heterocyclyl; D = bond, (substituted) alkyl, alkenyl, alkynyl; R2 = CO2H, (substituted) CO2H isostere], were prepd. Thus, L-proline Me ester hydrochloride in CH2Cl2 was treated with Et3N and then with MeO2CCOCl to give 88% Me (2S)-1-(1,2-dioxo-2-methoxyethyl)-2-pyrrolidinecarboxylate. The latter in THF at -78.degree. was treated with 1,1-dimethylpropylmagnesium chloride followed by 3 h stirring at -78.degree. to give 75% Me (2S)-1-(1,2-dioxo-3,3-dimethylpentyl)-2-pyrrolidinecarboxylate. This was stirred overnight with aq. LiOH in MeOH to give 87% (2S)-1-(1,2-dioxo-3,3-dimethylpentyl)-2-pyrrolidinecarboxylic acid. In the MPTP model of Parkinson's disease in mice, I at 10 mg/kg orally gave 10.4-46.5% recovery of TH-stained dopaminergic neurons.

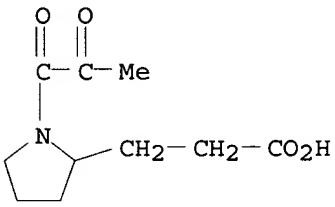
IT **251949-17-4P 251950-16-0P 251950-17-1P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of prolinylalkanediones and related compds. for treating neurol. disease, vision disorders, and alopecia)

RN 251949-17-4 CAPLUS
CN L-Proline, 1-(3,3-dimethyl-1,2-dioxobutyl)- (9CI) (CA INDEX NAME)

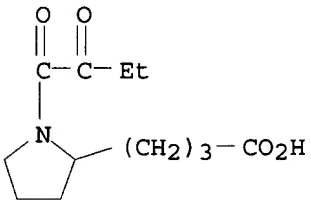
Absolute stereochemistry.



RN 251950-16-0 CAPLUS
CN 2-Pyrrolidinepropanoic acid, 1-(1,2-dioxopropyl)- (9CI) (CA INDEX NAME)



RN 251950-17-1 CAPLUS
CN 2-Pyrrolidinebutanoic acid, 1-(1,2-dioxobutyl)- (9CI) (CA INDEX NAME)



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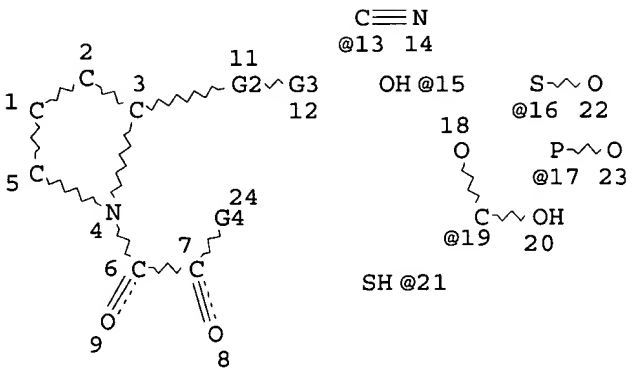
L28 HAS NO ANSWERS
L28 STR



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VAR G4=ME/ET/I-PR/N-PR/N-BU/I-BU/T-BU
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC 3
NUMBER OF NODES IS 23

STEREO ATTRIBUTES: NONE

=> s l28 ful
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FULL SCREEN SEARCH COMPLETED - 4528 TO ITERATE

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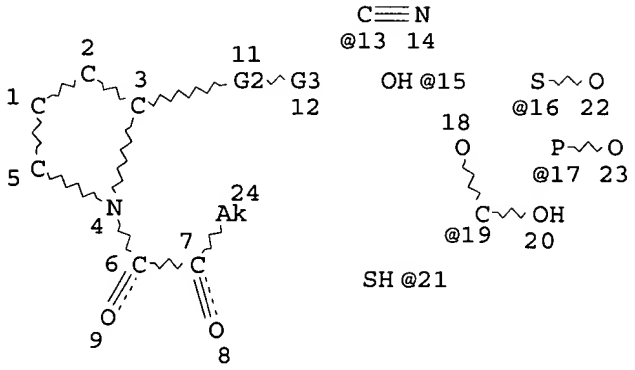
SEARCH TIME: 00.00.01

L30 16 SEA SSS FUL L28

=> d l31
L31 HAS NO ANSWERS
L31 STR



REP G2=(0-3) CH2
VAR G3=13/15/16/17/19/21
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC 3
NUMBER OF NODES IS 23

STEREO ATTRIBUTES: NONE

=> s l31 ful
FULL SEARCH INITIATED 11:10:05 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 11004 TO ITERATE

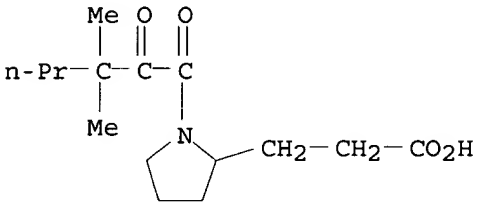
100.0% PROCESSED 11004 ITERATIONS 54 ANSWERS
SEARCH TIME: 00.00.01

L33 54 SEA SSS FUL L31

=> s l33 not l30
L34 38 L33 NOT L30

=> d scan

L34 38 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN 2-Pyrrolidinepropanoic acid, 1-(3,3-dimethyl-1,2-dioxohexyl)- (9CI)
MF C15 H25 N O4



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

AN 2001:247794 CAPLUS
DN 135:61281
TI Antimycobacterial Activity of Substituted Isosteres of Pyridine- and Pyrazinecarboxylic Acids. 2.
AU Gezginci, Mikail H.; Martin, Arnold R.; Franzblau, Scott G.
CS Department of Pharmacology and Toxicology College of Pharmacy, The University of Arizona, Tucson, AZ, 85721, USA
SO Journal of Medicinal Chemistry (2001), 44(10), 1560-1563
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English
AB **Pyridines** and pyrazines substituted with 1,2,4-oxadiazol-5-ones, 1,2,4-oxadiazole-5-thiones, and 1,3,4-oxathiazolin-2-ones were synthesized and tested against Mycobacterium tuberculosis. The two former ring systems were documented in the literature to act as **carboxylic acid isosteres**. The latter series was synthesized as possible synthetic intermediates to 1,2,4-thiadiazole-3-ones and was included in this study due to their interesting activity. Pivaloyloxymethyl derivs. of the isosteres were also prepd. in order to increase their lipophilicity and therefore improve their cellular permeability. The derivatized isosteres were expected to be bio-transformed by esterases to the active species after penetration of the mycobacterial cell wall. Biol. properties of the compds. were compared with the unmodified polar isosteres of pyrazinoic and nicotinic acids. The majority of the compds. exhibited activities ranging from 0.5 to 16 times the potency of pyrazinamide.
RE.CNT 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2003 ACS
AN 2000:133508 CAPLUS
DN 132:166514
TI heterocyclic carboxylic acid ureas or carbamates for vision and memory disorders.
IN Ross, Douglas T.; Sauer, Hansjorg; Hamilton, Gregory S.; Steiner, Joseph P.
PA Guilford Pharmaceuticals Inc., USA
SO PCT Int. Appl., 89 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2000009125	A1	20000224	WO 1999-US18234	19990812
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2336152	AA	20000224	CA 1999-2336152	19990812
AU 9954778	A1	20000306	AU 1999-54778	19990812
EP 1107754	A1	20010620	EP 1999-941054	19990812
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002522494	T2	20020723	JP 2000-564628	19990812
PRAI US 1998-134420	A	19980814		

AN 2001:247794 CAPLUS
DN 135:61281
TI Antimycobacterial Activity of Substituted Isosteres of Pyridine- and Pyrazinecarboxylic Acids. 2.
AU Gezginci, Mikail H.; Martin, Arnold R.; Franzblau, Scott G.
CS Department of Pharmacology and Toxicology College of Pharmacy, The University of Arizona, Tucson, AZ, 85721, USA
SO Journal of Medicinal Chemistry (2001), 44(10), 1560-1563
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English
AB **Pyridines** and pyrazines substituted with 1,2,4-oxadiazol-5-ones, 1,2,4-oxadiazole-5-thiones, and 1,3,4-oxathiazolin-2-ones were synthesized and tested against Mycobacterium tuberculosis. The two former ring systems were documented in the literature to act as **carboxylic acid isosteres**. The latter series was synthesized as possible synthetic intermediates to 1,2,4-thiadiazole-3-ones and was included in this study due to their interesting activity. Pivaloyloxymethyl derivs. of the isosteres were also prepd. in order to increase their lipophilicity and therefore improve their cellular permeability. The derivatized isosteres were expected to be bio-transformed by esterases to the active species after penetration of the mycobacterial cell wall. Biol. properties of the compds. were compared with the unmodified polar isosteres of pyrazinoic and nicotinic acids. The majority of the compds. exhibited activities ranging from 0.5 to 16 times the potency of pyrazinamide.
RE.CNT 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

AN 2001:247794 CAPLUS
DN 135:61281
TI Antimycobacterial Activity of Substituted Isosteres of Pyridine- and Pyrazinecarboxylic Acids. 2.
AU Gezginci, Mikail H.; Martin, Arnold R.; Franzblau, Scott G.
CS Department of Pharmacology and Toxicology College of Pharmacy, The University of Arizona, Tucson, AZ, 85721, USA
SO Journal of Medicinal Chemistry (2001), 44(10), 1560-1563
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English
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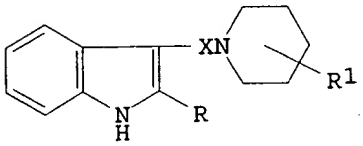
AN 1981:47062 CAPLUS
DN 94:47062
TI Synthesis and cardiovascular activity of piperidylethylindoles
AU Agarwal, Jagdish C.; Sharma, M.; Saxena, A. K.; Kishor, K.; Bhargava, K. P.; Shanker, K.
CS Dep. Pharmacol. Ther., King George's Med. Coll., Lucknow, India
SO Journal of the Indian Chemical Society (1980), 57(7), 742-3
CODEN: JICSAH; ISSN: 0019-4522
DT Journal
LA English
GI

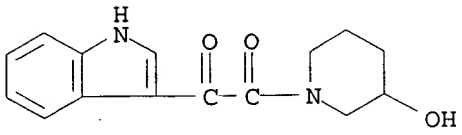


I, X=CH_2CH_2
II, X=COCO

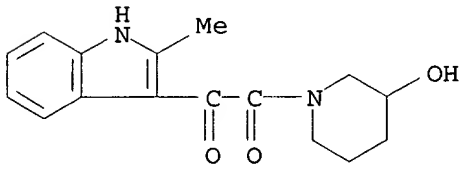
AB The piperidinoethylindoles I (R = H, Me, Ph; R1 = 2-Me, 3-Me, 4,4-Ph, HO) were prepd. by reaction of the corresponding piperidine with indoleglyoxylyl chloride to give II which were reduced with LiAlH4 to give I. Three compds. showed mild hypotensive activity and 2 compds. produced a short lasting hypertensive effect.

IT **71765-50-9P 71765-53-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and redn. of)

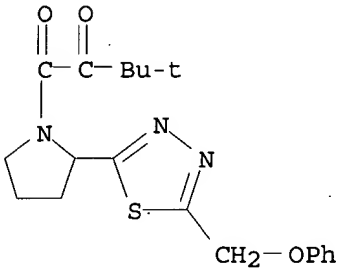
RN 71765-50-9 CAPLUS
CN 3-Piperidinol, 1-(1H-indol-3-yloxoacetyl)- (9CI) (CA INDEX NAME)



RN 71765-53-2 CAPLUS
CN 3-Piperidinol, 1-[(2-methyl-1H-indol-3-yl)oxoacetyl]- (9CI) (CA INDEX NAME)



RN **359803-05-7** REGISTRY
CN **Pyrrolidine, 1-(3,3-dimethyl-1,2-dioxobutyl)-2-[5-(phenoxymethyl)-1,3,4-thiadiazol-2-yl]- (9CI)** (CA INDEX NAME)
FS 3D CONCORD
MF C19 H23 N3 O3 S
SR CA
LC STN Files: CA, CAPLUS



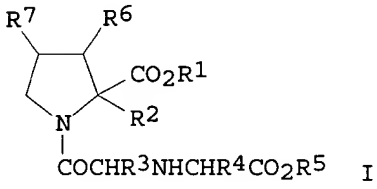
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

AN 1987:576479 CAPLUS
DN 107:176479
TI Preparation of alanylproline derivatives as antihypertensives
IN Weber, Wolf Dietrich; Gante, Joachim; Radunz, Hans Eckard; Schmitges, Claus; Minck, Klaus Otto
PA Merck Patent G.m.b.H., Fed. Rep. Ger.
SO Ger. Offen., 10 pp.
CODEN: GWXXBX
DT Patent
LA German
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 3536446	A1	19870416	DE 1985-3536446	19851012

PI
GI



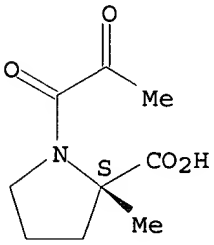
I

AB The title compds. [I; R1, R5 = H, alkyl, PhCH2; R2 = alkyl; R3 = Me, (CH2)4NH2; R4 = Me, CH2CH2Ar; R6, R7 = H or R6R7 = bond; Ar = (substituted) Ph] were prepd. as angiotensin converting enzyme inhibitors useful as antihypertensives (no data). DL-2-Methylproline tert-Bu ester, N-(1S-carboethoxy-3-phenylpropyl)-L-alanine.HCl, N-methylmorpholine, 1-hydroxybenzotriazole, and 1,3-dicyclohexylcarbodiimide were stirred for 3 h at 0.degree. to give, after salification with maleic acid, tert-Bu N-(1S-carboethoxy-3-phenylpropyl)-L-alanyl-L-2-methylproline maleate as a solid.

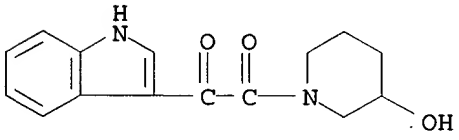
IT **110706-85-9**
RL: RCT (Reactant); RACT (Reactant or reagent)
(reductive amination of, by phenylaminobutyrate and sodium cyanoborohydride)

RN 110706-85-9 CAPLUS
CN L-Proline, 1-(1,2-dioxopropyl)-2-methyl- (9CI) (CA INDEX NAME)

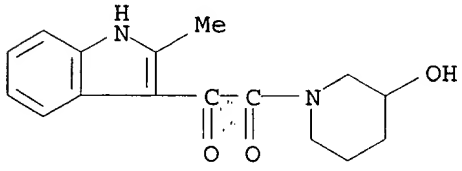
Absolute stereochemistry.



AN 1979:568360 CAPLUS
DN 91:168360
TI Pharmacological evaluation of some newer piperidyl ethyl indoles as anti-parkinsonian agent
AU Agarwal, Jagdish C.; Nath, C.; Sharma, M.; Kishor, K.; Shanker, K.; Gupta, G. P.; Bhargava, K. P.
CS Dep. Pharmacol. Ther., King George's Med. Coll., Lucknow, India
SO Indian Drugs (1979), 16(9), 209-12
CODEN: INDRBA; ISSN: 0019-462X
DT Journal
LA English
AB The antiparkinsonian and analgesic activities and the effects on locomotor activities of 23 indole derivs. were studied in rats and mice, and among these, 4 compds. antagonized oxotremorine-induced tremors, 10 antagonized reserpine-induced rigidity, and 1 decreased the locomotor activity, while 2 increased it. Only 2 compds. showed mild analgesic activity.
IT **71765-50-9 71765-53-2**
RL: BIOL (Biological study)
(as antiparkinsonian drug)
RN 71765-50-9 CAPLUS
CN 3-Piperidinol, 1-(1H-indol-3-yloxoacetyl)- (9CI) (CA INDEX NAME)

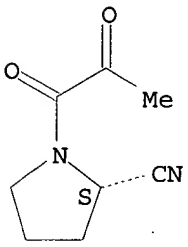


RN 71765-53-2 CAPLUS
CN 3-Piperidinol, 1-[(2-methyl-1H-indol-3-yl)oxoacetyl]- (9CI) (CA INDEX NAME)



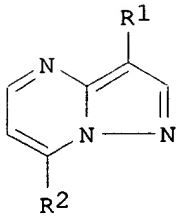
AN 1976:106021 CAPLUS
DN 84:106021
TI Efficient asymmetric synthesis of .alpha.-amino acids from .alpha.-keto acids and ammonia with conservation of the chiral reagent
AU Bycroft, Barrie W.; Lee, Grahame R.
CS Dep. Chem., Univ. Nottingham, Nottingham, Engl.
SO J. Chem. Soc., Chem. Commun. (1975), (24), 988-9
CODEN: JCCCAT
DT Journal
LA English
GI For diagram(s), see printed CA Issue.
AB (S)-proline Me ester with R1R2CHCOCO2H (R = R1 = H; R = H, R1 = CHMe2; R = Me, R1 = Et) gave the corresponding N-(.alpha.-oxoacyl) derivs. which cyclized with NH3 to give the 5-hydroxydioxopiperazines I. Dehydration of I gave II which was hydrogenated to the (S,S)-cyclodipeptides III. Hydrolysis of III gave L-RR1CHCH(NH2)CO2H and L-proline. L-MeCH(NHMe)CO2H was similarly prepd. using MeNH2 instead of NH3.
IT **58885-83-9P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 58885-83-9 CAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-(1,2-dioxopropyl)-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



AN 2001:247794 CAPLUS
DN 135:61281
TI Antimycobacterial Activity of Substituted Isosteres of Pyridine- and Pyrazinecarboxylic Acids. 2.
AU Gezginci, Mikail H.; Martin, Arnold R.; Franzblau, Scott G.
CS Department of Pharmacology and Toxicology College of Pharmacy, The University of Arizona, Tucson, AZ, 85721, USA
SO Journal of Medicinal Chemistry (2001), 44(10), 1560-1563
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English
AB Pyridines and pyrazines substituted with 1,2,4-oxadiazol-5-ones, 1,2,4-oxadiazole-5-thiones, and 1,3,4-oxathiazolin-2-ones were synthesized and tested against Mycobacterium tuberculosis. The two former ring systems were documented in the literature to act as carboxylic acid isosteres. The latter series was synthesized as possible synthetic intermediates to 1,2,4-thiadiazole-3-ones and was included in this study due to their interesting activity. Pivaloyloxymethyl derivs. of the isosteres were also prepd. in order to increase their lipophilicity and therefore improve their cellular permeability. The derivatized isosteres were expected to be bio-transformed by esterases to the active species after penetration of the mycobacterial cell wall. Biol. properties of the compds. were compared with the unmodified polar isosteres of pyrazinoic and nicotinic acids. The majority of the compds. exhibited activities ranging from 0.5 to 16 times the potency of pyrazinamide.
RE.CNT 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

AN 121:300841 CA
TI **Oxadiazoles** as **bioisosteric** transformations of **carboxylic** functionalities. Part I
AU Andersen, K. E.; Joergensen, A. S.; Braestrup, C.
CS Novo Nordisk, A/S, CNS Division, Maaloev, 2760, Den.
SO Eur. J. Med. Chem. (1994), 29(5), 393-9
CODEN: EJMCA5; ISSN: 0223-5234
DT Journal
LA English
OS CASREACT 121:300841
GI



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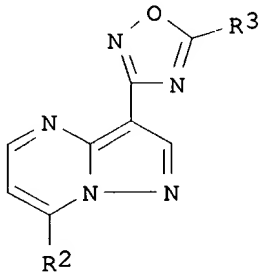


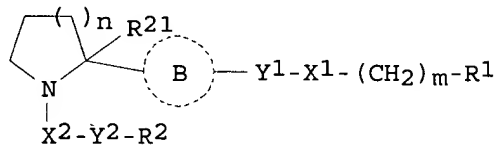
II

AB Cyclocondensation of aminopyrazoles with appropriate 3-(dimethylamino)-1-aryl-2-propen-1-ones gave 51-86% pyrazolo[1,5-a]pyrimidines I (R1 = cyano, CO2Et, R2 = 4-F3CC6H4, Ph, 3-thienyl, etc.). Reaction of nitriles I with hydroxylamine in aq. ethanol gave crude 56-93% amidoximes which on heating with an acid chloride or anhydride afforded 65-81% oxadiazole derivs. II (R3 = Me, cyclopropyl, CF3, R2 = same). Some pyrrolopyrimidines were also prepd. and the prepd. compds. were tested as benzodiazepine receptors.

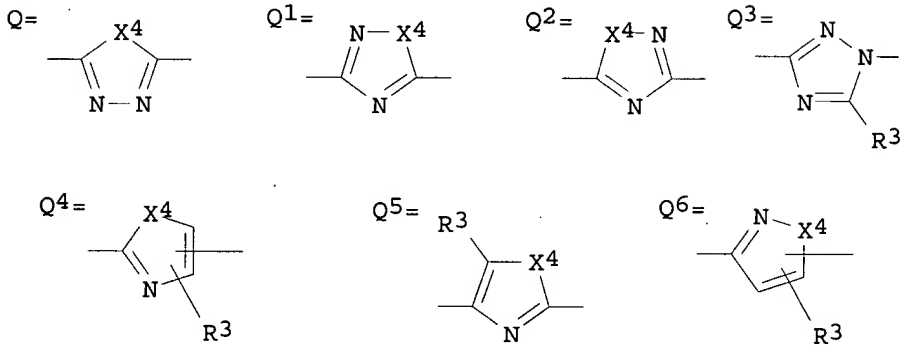
AN 2001:668212 CAPLUS
DN 135:226999
TI Preparation of 2-azolylpyrrolidine or -piperidine derivatives having neurite outgrowth activity
IN Kato, Susumu; Ueno, Hiroshi; Kondo, Wataru
PA Japan Tobacco, Inc., Japan
SO Jpn. Kokai Tokkyo Koho, 81 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI JP 2001247569	A2	20010911	JP 2000-236882	20000804
PRAI JP 1999-228938	A	19990812		
JP 1999-375867	A	19991228		

OS MARPAT 135:226999
GI



I



AB The title compds. [I; R1 = H, (un)substituted C3-10 cycloalkyl, C6-12 aryl, or 5- to 6-membered heterocyclyl contg. 1-3 heteroatoms selected from O, S, and N; R2 = C1-6 alkyl, C3-10 cycloalkyl, C6-12 aryl, or 5- to 6-membered heterocyclyl contg. 1-3 heteroatoms selected from O, S, and N; R21 = H, C1-6 alkyl; X1 = single bond, O, S, SO, SO2, CH:CH, CO, CO2, NR10, CONR10, NR10CO, NR11CONR10, NR10SO2, SO2NR10, CR10R11 [wherein R10 = H, (CH2)nR12 (wherein n = 1-4; R12 = C3-10 cycloalkyl, C6-12 aryl, or 5- to 6-membered heterocyclyl contg. 1-3 heteroatoms selected from O, S, and N); R11 = H, C1-6 alkyl]; Y1 = arylene, heteroarylene, (CH2)p (wherein p = 0, 1-4); X2 = SO2, COCO, CO2, CO, C(S), CONR14, C(S)NR14 (wherein R14 = H, C1-6 alkyl); Y = (CH2)r (wherein r = 0, 1-3), CH:CH; m = 0, 1-4; ring B = Q - Q6 [wherein R3 = H, C1-6 alkyl; X4 = O, S, NR4 (wherein R4 = H, C1-6 alkyl)], (un)substituted condensed heterocyclyl], salts thereof, or their hydrates or prodrugs are prepd. These compds. are superior in serum stability and can be administered orally and are useful for the treatment and/or prevention of diseases accompanied by nerve injury or neurodegeneration, e.g. diabetic nerve disorders, neuropathy, nerve cutting, amyotrophic lateral sclerosis (ALC), multiple sclerosis, Alzheimer's diseases, Parkinson's diseases, Huntington chorea, and spinal code injury. Thus, 464 mg 7-chloronaphth-2-ylsulfonyl chloride was added

to a soln. of 507 mg 5-(5-benzyloxycarbonylaminomethyl-1,3,4-thiadiazol-2-yl)pyrrolidine (prepn. given) in pyridine and stirred at room temp. for 3 h to give 706 mg 1-(7-chloronaphthalen-2-ylsulfonyl)-2-(5-benzyloxycarbonylaminomethyl-1,3,4-thiadiazol-2-yl)pyrrolidine which (678 mg) was treated with 25% HBr-AcOH at room temp. for 1 h and treated with diisopropyl ether for pptg. crystals, followed by neutralizing the pptd. crystals with 1 N aq. NaOH and extn. with CH2Cl2 to give 472 mg 1-(7-chloronaphthalen-2-ylsulfonyl)-2-(5-aminomethyl-1,3,4-thiadiazol-2-yl)pyrrolidine. To a soln. of the latter compd. (164 mg) in 2 mL pyridine was added 143 mg nicotinoyl chloride hydrochloride and stirred at room temp. for 30 min to give 183 mg N-[5-[1-(7-chloronaphthalene-2-sulfonyl)pyrrolidin-2-yl]-1,3,4-thiadiazol-2-yl]methyl-3-pyridinecarboxamide (II). II at 10 nM in vitro exhibited the enhancement of the NGF-induced neurite outgrowth in PC12h cells equiv. to that of 100 nM FK-506.

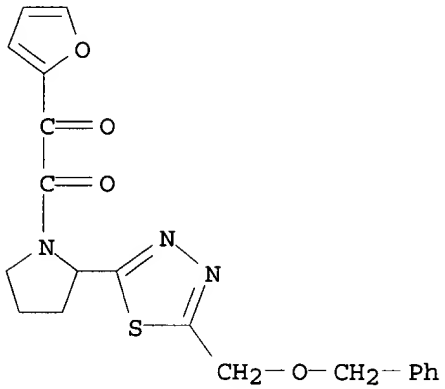
IT **359802-65-6P 359802-83-8P 359803-05-7P 359803-06-8P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of 2-azolylpyrrolidine or -piperidine derivs. having neurite outgrowth activity for treatment and/or prevention of nerve injury or neurodegenerative diseases)

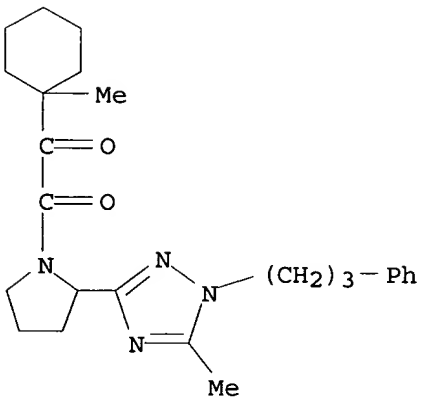
RN 359802-65-6 CAPLUS

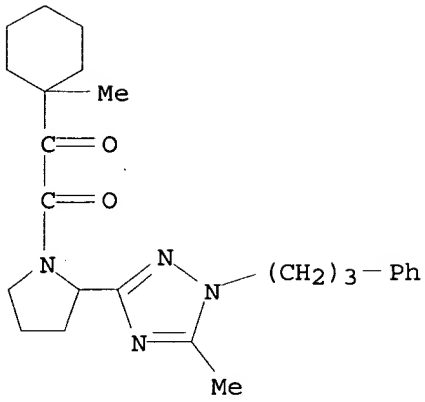
CN Pyrrolidine, 1-(2-furanyloxoacetyl)-2-[5-[(phenylmethoxy)methyl]-1,3,4-thiadiazol-2-yl]- (9CI) (CA INDEX NAME)



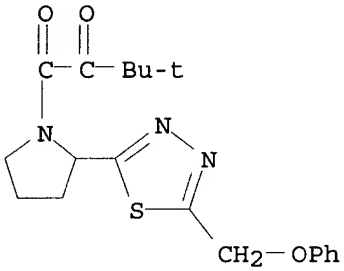
RN 359802-83-8 CAPLUS

CN Pyrrolidine, 1-[(1-methylcyclohexyl)oxoacetyl]-2-[5-methyl-1-(3-phenylpropyl)-1H-1,2,4-triazol-3-yl]- (9CI) (CA INDEX NAME)

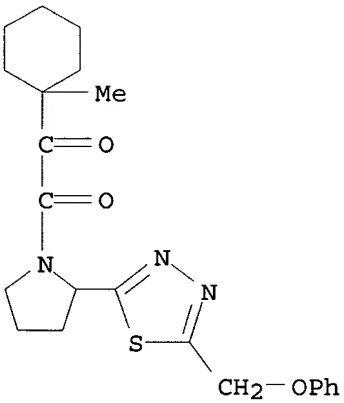




RN 359803-05-7 CAPLUS
CN Pyrrolidine, 1-(3,3-dimethyl-1,2-dioxobutyl)-2-[5-(phenoxymethyl)-1,3,4-thiadiazol-2-yl]- (9CI) (CA INDEX NAME)



RN 359803-06-8 CAPLUS
CN Pyrrolidine, 1-[(1-methylcyclohexyl)oxoacetyl]-2-[5-(phenoxymethyl)-1,3,4-thiadiazol-2-yl]- (9CI) (CA INDEX NAME)



AN 1999:784078 CAPLUS
DN 132:22860
TI Preparation of aza-heterocyclic compounds used to treat neurological disorders and hair loss
IN Hamilton, Gregory S.; Norman, Mark H.; Wu, Yong-Qian; Steiner, Joseph P.
PA Guilford Pharmaceuticals Inc., USA; Amgen, Inc.
SO PCT Int. Appl., 96 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 5

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9962881	A1	19991209	WO 1998-US25573	19981203
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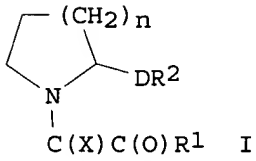
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	CA 2333963	AA	19991209	CA 1998-2333963	19981203
	AU 9917081	A1	19991220	AU 1999-17081	19981203
	ZA 9811063	A	20000707	ZA 1998-11063	19981203
	BR 9815920	A	20010220	BR 1998-15920	19981203
	EP 1084107	A1	20010321	EP 1998-961866	19981203
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	JP 2002516905	T2	20020611	JP 2000-552093	19981203
	NO 2000005903	A	20010202	NO 2000-5903	20001121
PRAI	US 1998-87788P	P	19980603		
	US 1998-101077P	P	19980918		
	WO 1998-US25573	W	19981203		

OS MARPAT 132:22860
GI



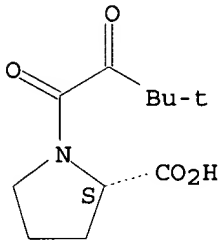
I

AB Prepn. of N-heterocyclic carboxylic acids and carboxylic acid isosteres I [n = 1-3; X = O, S; R1 = C1-C9 straight or branched chain alkyl, C2-C9 straight or branched chain alkenyl, aryl, heteroaryl, carboncycle, heterocycle; D = bond, C1-C10 straight or branched chain alkyl, C2-C10 alkenyl, C2-C10 alkynyl; R2 = carboxylic acid, carboxylic acid isostere] and their use for treating neurol. disorders and for treating alopecia and promoting hair growth are described. E.g., (2S)-1-(1,2-dioxo-3,3-dimethylpentyl)-2-hydroxymethylpyrrolidine was prepd.

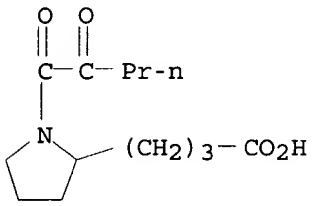
IT **251949-17-4P 251949-47-0P 251950-16-0P**
251950-17-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of aza-heterocyclic compds. used to treat neurol. disorders and hair loss)

RN 251949-17-4 CAPLUS
CN L-Proline, 1-(3,3-dimethyl-1,2-dioxobutyl)- (9CI) (CA INDEX NAME)

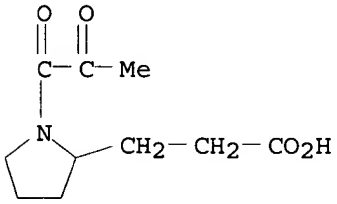
Absolute stereochemistry.



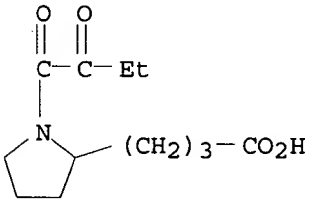
RN 251949-47-0 CAPLUS
CN 2-Pyrrolidinebutanoic acid, 1-(1,2-dioxopentyl)- (9CI) (CA INDEX NAME)



RN 251950-16-0 CAPLUS
CN 2-Pyrrolidinepropanoic acid, 1-(1,2-dioxopropyl)- (9CI) (CA INDEX NAME)



RN 251950-17-1 CAPLUS
CN 2-Pyrrolidinebutanoic acid, 1-(1,2-dioxobutyl)- (9CI) (CA INDEX NAME)



RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

AN 1998:503787 CAPLUS
DN 129:226091
TI TGF-.beta.-signaling with small molecule FKBP12 antagonists that bind myristoylated FKBP12-TGF-.beta. type I receptor fusion proteins
AU Stockwell, Brent R.; Schreiber, Stuart L.
CS Howard Hughes Medical Inst., Dep. Chem. Chem. Biol., Harvard Univ., Cambridge, MA, 02138, USA
SO Chemistry & Biology (1998), 5(7), 385-395
CODEN: CBOLE2; ISSN: 1074-5521
PB Current Biology Ltd.
DT Journal
LA English
AB Growth arrest in many cell types is triggered by transforming growth factor beta (TGF-.beta.), which signals through two TGF-.beta. receptors (type I, TGF-.beta.RI, and type II, TGF-.beta.RII). In the signaling pathway, TGF-.beta. binds to the extracellular domain of TGF-.beta.RII, which can then transphosphorylate TGF-.beta.RI in its glycine/serine (GS)-rich box. Activated TGF-.beta.RI phosphorylates two downstream effectors, Smad2 and Smad3, leading to their translocation into the nucleus. Cell growth is arrested and plasminogen activator inhibitor 1 (PAI-1) is upregulated. The authors investigated the role of the **immunophilin** FKBP12, which can bind to the GS box of TGF-.beta.RI, in TGF-.beta. signaling. Overexpression of myristoylated TGF-.beta.RI and TGF-.beta.RII cytoplasmic tails caused constitutive nuclear translocation of a green-fluorescent-protein-Smad2 construct in COS-1 cells, and constitutive activation of a PAI-1 reporter plasmid in mink lung cells. Fusing FKBP12 to TGF-.beta.RI resulted in repression of autosignaling that could be alleviated by FK506M or rapamycin (two small mols. that can bind to FKBP12). Mutation of the FKBP12-binding site in the FKBP12-TGF-.beta.RI fusion protein restored constitutive signaling. An **acidic** mutation in the FKBP12-TGF.beta.RI protein allowed FKBP12 antagonists to activate signaling in the absence of TGF-.beta.RII. Further mutations in the TGF-.beta.RI FKBP12-binding site resulted in TGF-.beta. signaling that was independent of both TGF-.beta.RII and FKBP12 antagonists. Fusing FKBP12 to TGF-.beta.RI results in a novel receptor that is activated by small mol. FKBP12 antagonists. These results suggest that FKBP12 binding to TGF-.beta.RI is inhibitory and that FKBP12 plays a role in inhibiting TGF-.beta. superfamily signals.
RE.CNT 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
AB Growth arrest in many cell types is triggered by transforming growth factor beta (TGF-.beta.), which signals through two TGF-.beta. receptors (type I, TGF-.beta.RI, and type II, TGF-.beta.RII). In the signaling pathway, TGF-.beta. binds to the extracellular domain of TGF-.beta.RII, which can then transphosphorylate TGF-.beta.RI in its glycine/serine (GS)-rich box. Activated TGF-.beta.RI phosphorylates two downstream effectors, Smad2 and Smad3, leading to their translocation into the nucleus. Cell growth is arrested and plasminogen activator inhibitor 1 (PAI-1) is upregulated. The authors investigated the role of the **immunophilin** FKBP12, which can bind to the GS box of TGF-.beta.RI, in TGF-.beta. signaling. Overexpression of myristoylated TGF-.beta.RI and TGF-.beta.RII cytoplasmic tails caused constitutive nuclear translocation of a green-fluorescent-protein-Smad2 construct in COS-1 cells, and constitutive activation of a PAI-1 reporter plasmid in mink lung cells. Fusing FKBP12 to TGF-.beta.RI resulted in repression of autosignaling that could be alleviated by FK506M or rapamycin (two small mols. that can bind to FKBP12). Mutation of the FKBP12-binding site in the FKBP12-TGF-.beta.RI fusion protein restored constitutive signaling. An **acidic** mutation in the FKBP12-TGF.beta.RI protein allowed FKBP12 antagonists to activate signaling in the absence of TGF-.beta.RII. Further mutations in the TGF-.beta.RI FKBP12-binding site resulted in TGF-.beta. signaling that was independent of both TGF-.beta.RII and FKBP12

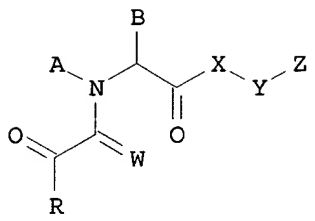
antagonists. Fusing FKBP12 to TGF-.beta.RI results in a novel receptor that is activated by small mol. FKBP12 antagonists. These results suggest that FKBP12 binding to TGF-.beta.RI is inhibitory and that FKBP12 plays a role in inhibiting TGF-.beta. superfamily signals.

IT Protein motifs
(leucine-**proline**; TGF-.beta.-signaling with small mol. FKBP12 antagonists that bind myristoylated FKBP12-TGF-.beta. type I receptor fusion proteins)

AN 1998:603244 CAPLUS
DN 129:230649
TI Preparation of N-oxides of heterocyclic esters, amides, thioesters, and ketones as inhibitors of the enzyme activity assocd. with immunophilin proteins
IN **Hamilton, Gregory S.**; Steiner, Joseph P.; Burak, Eric S.
PA Guilford Pharmaceuticals Inc., USA
SO PCT Int. Appl., 67 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9837885	A1	19980903	WO 1998-US3484	19980226
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	US 5846979	A	19981208	US 1997-807406	19970228
	CA 2229707	AA	19980828	CA 1998-2229707	19980216
	ZA 9801474	A	19980608	ZA 1998-1474	19980223
	AU 9861815	A1	19980918	AU 1998-61815	19980226
	AU 723374	B2	20000824		
	EP 993299	A1	20000419	EP 1998-906646	19980226
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	JP 10310581	A2	19981124	JP 1998-64463	19980227
	TW 458976	B	20011011	TW 1998-87102828	19980424
	US 6054452	A	20000425	US 1998-112319	19980709
	US 6251892	B1	20010626	US 2000-556482	20000421
	US 2001036942	A1	20011101	US 2001-842174	20010426
	US 6486151	B2	20021126		
PRAI	US 1997-807406	A	19970228		
	WO 1998-US3484	W	19980226		
	US 1998-112319	A1	19980709		
	US 2000-556482	A1	20000421		

OS MARPAT 129:230649
GI



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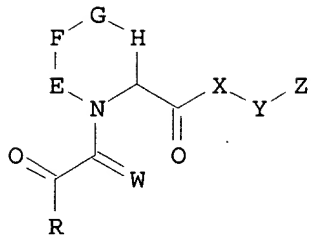
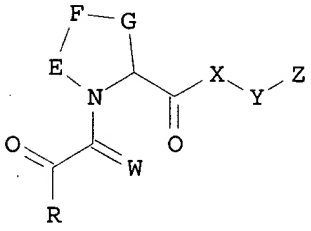
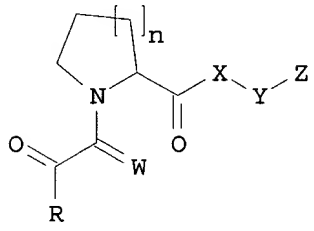


II



III



IV

AB The title compds. [I-IV; A and B, together with N and C atoms to which they are attached, = (un)satd. 5-7 membered hetrocyclyl; E, F, G and H = CH2, O, S, etc.; W = O, S, CH2, H2; R = C1-6 alkyl, C1-6 alkenyl, etc.; X = O, NH, S, etc.; Y = a direct bond, C1-6 alkyl, C1-6 alkenyl, etc.; Z = an arom. or tertiary alkyl amine oxidized to a corresponding N-oxide; n = 1-3], having an affinity for FKBP-type immunophilins, and therefore useful as inhibitors of the enzyme activity assocd. with immunophilin proteins, particularly peptidyl-prolyl isomerase, or rotamase activity, were prepd. Thus, 5-step synthesis of (S)-IV [X = O; Y = (CH2)3; Z = 3-pyridyl N-oxide; R = 1,1-dimethylpentyl; n = 1], which showed Ki of 225 nM against **esterase** degrdn., is described.

RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

IN **Hamilton, Gregory S.**; Steiner, Joseph P.; Burak, Eric S.

AB The title compds. [I-IV; A and B, together with N and C atoms to which they are attached, = (un)satd. 5-7 membered hetrocyclyl; E, F, G and H = CH2, O, S, etc.; W = O, S, CH2, H2; R = C1-6 alkyl, C1-6 alkenyl, etc.; X = O, NH, S, etc.; Y = a direct bond, C1-6 alkyl, C1-6 alkenyl, etc.; Z = an arom. or tertiary alkyl amine oxidized to a corresponding N-oxide; n = 1-3], having an affinity for FKBP-type immunophilins, and therefore useful as inhibitors of the enzyme activity assocd. with immunophilin proteins, particularly peptidyl-prolyl isomerase, or rotamase activity, were prepd. Thus, 5-step synthesis of (S)-IV [X = O; Y = (CH2)3; Z = 3-pyridyl N-oxide; R = 1,1-dimethylpentyl; n = 1], which showed Ki of 225 nM against **esterase** degrdn., is described.

AN 2000:553576 CAPLUS
DN 133:164058
TI Preparation of 1-gloxyloyl-2-heteroarylpyrrolidines as nerve growth stimulants
IN Brumby, Thomas; McDonald, Fiona; Ottow, Eckhard; Schneider, Herbert
PA Schering Aktiengesellschaft, Germany; Vertex Pharmaceuticals, Inc.
SO PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000046222	A1	20000810	WO 2000-US2660	20000203
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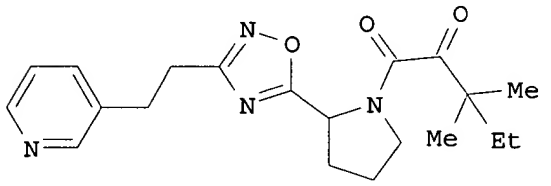
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	DE 19905256	A1	20000810	DE 1999-19905256	19990203
	US 6284779	B1	20010904	US 2000-496278	20000201
PRAI	DE 1999-19905256	A	19990203		
	US 1999-126007P	P	19990324		
	US 2000-496278	A	20000201		

OS MARPAT 133:164058
GI



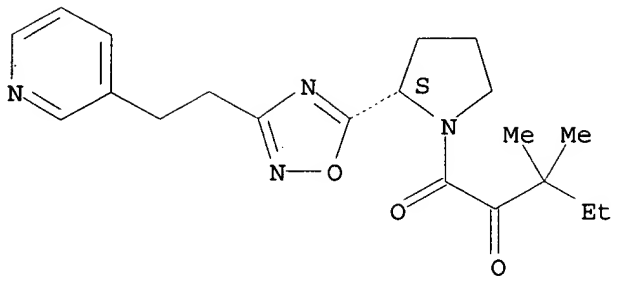
I

AB R1Z1NR2CHR3ZR4 [R1 = H, alkyl, (hetero)aryl(alkyl), etc.; R2 = (phenyl)alkyl, halophenylalkyl; R3 = (cyclo)alk(en)yl, phenyl[alk(en)yl], etc.; R2R3 = atoms to complete a ring; R4 = (cyclo)alk(en)yl, phenyl[alk(en)yl], etc.; Z = 5-membered heteroarylene; Z1 = COCO, CO2, SO2, CONH, etc.] were prepd as nerve growth stimulants (no data). Thus, pyridine-3-carboxaldehyde was condensed with (EtO)2P(O)CH2CN and the hydrogenated product condensed with HONH2 to give RCH2CH2C(:NOH)NH2 (R = 3-pyridinyl) which was cyclocondensed with Boc-proline to give, in 3 addnl. steps, title compd. (S)-I.

IT **287963-66-0P 287963-67-1P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of 1-gloxyloyl-2-heteroarylpyrrolidines as nerve growth stimulants)

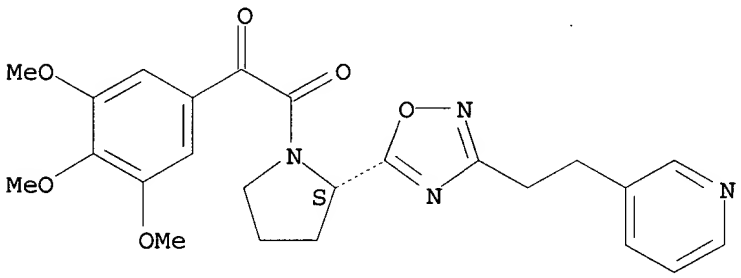
RN 287963-66-0 CAPLUS
CN Pyrrolidine, 1-(3,3-dimethyl-1,2-dioxopentyl)-2-[3-[2-(3-pyridinyl)ethyl]-1,2,4-oxadiazol-5-yl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



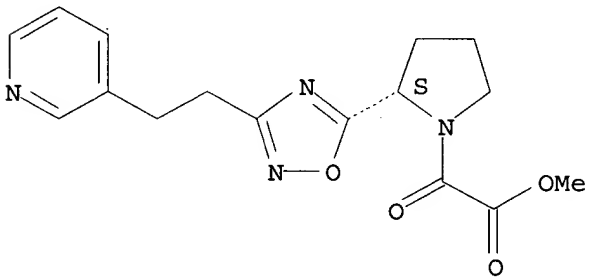
RN 287963-67-1 CAPLUS
CN Pyrrolidine, 1-[oxo(3,4,5-trimethoxyphenyl)acetyl]-2-[3-[2-(3-pyridinyl)ethyl]-1,2,4-oxadiazol-5-yl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



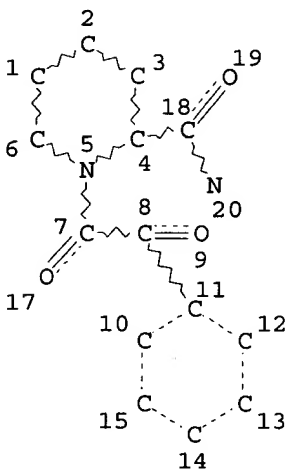
IT **287963-71-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of 1-gloxyloyl-2-heteroarylpyrrolidines as nerve growth stimulants)
RN 287963-71-7 CAPLUS
CN 1-Pyrrolidineacetic acid, .alpha.-oxo-2-[3-[2-(3-pyridinyl)ethyl]-1,2,4-oxadiazol-5-yl]-, methyl ester, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d l5
L5 HAS NO ANSWERS
L5 STR



NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC 5
NUMBER OF NODES IS 19

STEREO ATTRIBUTES: NONE

=> s l5 ful
FULL SEARCH INITIATED 09:58:31 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 619 TO ITERATE

100.0% PROCESSED 619 ITERATIONS 6 ANSWERS
SEARCH TIME: 00.00.01

L7 6 SEA SSS FUL L5

=> fil caplus
COST IN U.S. DOLLARS

	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	142.94	143.36

FILE 'CAPLUS' ENTERED AT 09:58:36 ON 04 DEC 2002
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 4 Dec 2002 VOL 137 ISS 23
FILE LAST UPDATED: 3 Dec 2002 (20021203/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

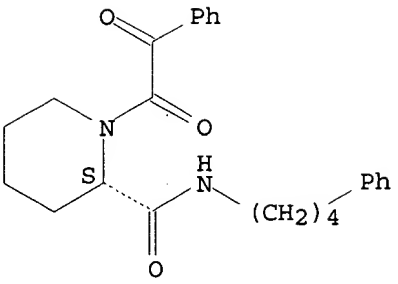
CAS roles have been modified effective December 16, 2001. Please check your SDI profiles to see if they need to be revised. For information on CAS roles, enter HELP ROLES at an arrow prompt or use the CAS Roles thesaurus (/RL field) in this file.

=> s l7
L8 6 L7

=> d bib abs hitstr 1-6

L8 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2002 ACS
AN 2002:515544 CAPLUS
DN 137:201562
TI Synthesis of N-Glyoxyl Prolyl and Pipecolyl Amides and Thioesters and Evaluation of Their In Vitro and In Vivo Nerve Regenerative Effects
AU Hamilton, Gregory S.; Wu, Yong-Qian; Limburg, David C.; Wilkinson, Douglas E.; Vaal, Mark J.; Li, Jia-He; Thomas, Christine; Huang, Wei; Sauer, Hansjorg; Ross, Douglas T.; Soni, Raj; Chen, Yi; Guo, Hongshi; Howorth, Pamela; Valentine, Heather; Liang, Shi; Spicer, Dawn; Fuller, Mike; Steiner, Joseph P.
CS Department of Research, Guilford Pharmaceuticals Inc., Baltimore, MD, 21224, USA
SO Journal of Medicinal Chemistry (2002), 45(16), 3549-3557
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English
AB The recent discovery that small mol. ligands for the peptidyl-prolyl isomerase (PPIase) FKBP12 possess powerful neuroprotective and neuroregenerative properties in vitro and in vivo suggests therapeutic utility for such compds. in neurodegenerative disease. The neurotrophic effects of these compds. are independent of the immunosuppressive pathways by which drugs such as FK506 and rapamycin operate. Previous work by the authors and other groups exploring the structure-activity relationships (SAR) of small mols. that mimic only the FKBP binding domain portion of FK506 has focused on esters of proline and pipecolic acid. The authors have explored amide and thioester analogs of these earlier structures and found that they too are extremely potent in promoting recovery of lesioned dopaminergic pathways in a mouse model of Parkinson's disease. Several compds. were shown to be highly effective upon oral administration after lesioning of the dopaminergic pathway, providing further evidence of the potential clin. utility of a variety of structural classes of FKBP12 ligands.
IT **409366-88-7P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. of N-glyoxylprolyl- and N-glyoxylpipecolyl-amides and thioesters and evaluation of their neurotrophic effects as inhibitors of peptidyl-prolyl isomerase)
RN 409366-88-7 CAPLUS
CN 2-Piperidinecarboxamide, 1-(oxophenylacetyl)-N-(4-phenylbutyl)-, (2S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

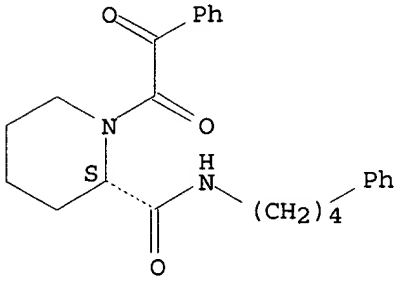
L8 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2002 ACS
AN 2002:332684 CAPLUS
DN 136:340999
TI Preparation of amino acid derivatives as rotamase enzyme activity inhibitors
IN Steiner, Joseph P.; Hamilton, Gregory S.
PA USA
SO U.S. Pat. Appl. Publ., 40 pp., Cont.-in-part of U.S. Ser. No. 359,351.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 8

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2002052410	A1	20020502	US 2001-805249	20010314
	US 5614547	A	19970325	US 1995-479436	19950607
	US 2002013344	A1	20020131	US 1995-551026	19951031
PRAI	US 1995-479436	A1	19950607		
	US 1995-551026	A2	19951031		
	US 1996-693003	B1	19960806		
	US 1999-359351	A2	19990721		

OS MARPAT 136:340999
AB The invention relates to methods of using neurotrophic compds. having an affinity for FKBP-type immunophilins to stimulate or promote neuronal growth or regeneration and to prevent neuronal degeneration. Amino acid derivs. R1C(:X)CON(J)CHKCO-Y(CH2)nCHZR2 [n = 0-3; Y is CH2, O, NH, or alkylimino; Z and R2 are independently Ar, or cycloalkyl, cycloalkenyl, or Ar-(un)substituted alkyl or alkenyl, or TCH:C(Q)CH2-, where Q = H, alkyl or alkenyl; T is Ar or substituted cycloalkyl; Ar is an (un)substituted mono or bicyclic heterocyclic arom. ring; R1 is U, where U is H, (un)substituted alkyl, alkoxy, alkenyl, alkenyloxy, cycloalkyl or cycloalkenyl; X is O or CH-U , provided that if R1 is H, then X is CH-U or if X is O then R1 is U; J is H, alkyl or benzyl; K is alkyl, benzyl or cyclohexylethyl; or J and K may be taken together to form a 5-7 membered heterocyclic ring which may contain O, S, SO or SO2] or their pharmaceutically acceptable salts are claimed. Thus, 3-(3,4,5-trimethoxyphenyl)propyl (2S)-1-(3,3-dimethyl-1,2-dioxopentyl)-2-pyrrolidinecarboxylate was prepd. by esterification of the acid and showed Ki = 0.025 .mu.M for inhibition of rotamase and ED50 = 80 nM for neurite outgrowth in chick dorsal root ganglion (DRG) cultures.
IT **409366-88-7P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of glyoxalylprolinate and -pipecolinate derivs. as rotamase inhibitors)
RN 409366-88-7 CAPLUS
CN 2-Piperidinecarboxamide, 1-(oxophenylacetyl)-N-(4-phenylbutyl)-, (2S)-

(9CI) (CA INDEX NAME)

Absolute stereochemistry.



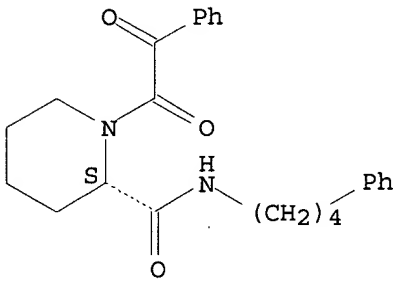
L8 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2002 ACS
AN 2002:276521 CAPLUS
DN 136:310178
TI Preparation of amino acid derivatives as rotamase enzyme activity inhibitors
IN Steiner, Joseph P.; Hamilton, Gregory S.
PA USA
SO U.S. Pat. Appl. Publ., 39 pp., Cont.-in-part of U.S. Ser. No. 551,026.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 8

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2002042377	A1	20020411	US 2001-873298	20010605
	US 5614547	A	19970325	US 1995-479436	19950607
	US 2002013344	A1	20020131	US 1995-551026	19951031
PRAI	US 1995-479436	A1	19950607		
	US 1995-551026	A2	19951031		
	US 1996-693003	B1	19960806		
	US 1999-359351	A2	19990721		

OS MARPAT 136:310178
AB The invention relates to methods of using neurotrophic compds. having an affinity for FKBP-type immunophilins to stimulate or promote neuronal growth or regeneration and to prevent neuronal degeneration. Amino acid derivs. R1C(:X)CON(J)CHKCO-Y-Z [Y is O, NH, or alkylimino; Z is H, CHL-Ar, alkyl, alkenyl, cycloalkyl, cycloalkenyl or Ar-substituted alkyl or alkenyl, or TCH:C(Q)CH(L)-, where L and Q are H, alkyl or alkenyl; T is Ar or substituted cyclohexyl; Ar is 1- or 2-naphthyl, 2- or 3-furyl, 2-thienyl, 2-, 3- or 4-pyridyl, (un)substituted phenyl; R1 is U, where U is H, (un)substituted alkyl, alkoxy, alkenyl, alkenyloxy, cycloalkyl or cycloalkenyl; X is O or CH-U , provided that if R1 is H, then X is CH-U or if X is O then R1 is U; J is H, alkyl or benzyl; K is alkyl, benzyl or cyclohexylethyl; or J and K may be taken together to form a 5-7 membered heterocyclic ring which may contain O, S, SO or SO2] or their pharmaceutically acceptable salts are claimed. Thus, 3-(3,4,5-trimethoxyphenyl)propyl (2S)-1-(3,3-dimethyl-1,2-dioxopentyl)-2-pyrrolidinecarboxylate was prepd. by esterification of the acid and showed Ki = 0.025 .mu.M for inhibition of rotamase and ED50 = 80 nM for neurite outgrowth in chick dorsal root ganglion (DRG) cultures.
IT **409366-88-7P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of glyoxalylprolinate and -pipecolinate derivs. as rotamase inhibitors)

RN 409366-88-7 CAPLUS
CN 2-Piperidinecarboxamide, 1-(oxophenylacetyl)-N-(4-phenylbutyl)-, (2S)-
(9CI) (CA INDEX NAME)

Absolute stereochemistry.



L8 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2002 ACS
AN 2000:227463 CAPLUS
DN 132:269827
TI Method of treating hair loss using ketoamides
IN Tiesman, Jay Patrick; Fulmer, Andrew Wayne; McIver, John Mcmillan; Degenhardt, Charles Raymond; Eickhoff, David Joseph
PA The Procter & Gamble Company, USA
SO PCT Int. Appl., 71 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

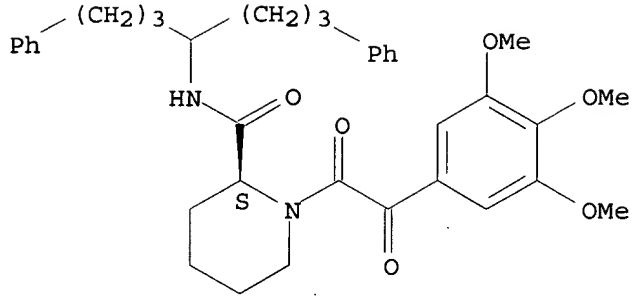
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000018358	A2	20000406	WO 1999-US22215	19990924
	WO 2000018358	A3	20000727		
	W: AU, BR, CA, CN, JP, MX				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	AU 9960602	A1	20000417	AU 1999-60602	19990924
	BR 9914197	A	20010703	BR 1999-14197	19990924
	EP 1117371	A2	20010725	EP 1999-969666	19990924
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	JP 2002525302	T2	20020813	JP 2000-571880	19990924
PRAI	US 1998-102458P	P	19980930		
	WO 1999-US22215	W	19990924		

AB The present disclosure describes methods for treating hair loss in mammals, including arresting and/or reversing hair loss and promoting hair growth. The methods comprise administering a pyrrolidinyl or piperidinyl ketoamide and a pharmaceutically-acceptable carrier. (S)-N-(3,4,5-trimethoxyphenylglyoxyl)pipecolic acid 1,7-diphenyl-4-heptylamide was prepd. and incorporated into a topical compn.

IT **263239-96-9P**
RL: BUU (Biological use, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(treating hair loss using ketoamides)

RN 263239-96-9 CAPLUS
CN 2-Piperidinecarboxamide, 1-[oxo(3,4,5-trimethoxyphenyl)acetyl]-N-[4-phenyl-1-(3-phenylpropyl)butyl]-, (2S)- (9CI) (CA INDEX NAME)

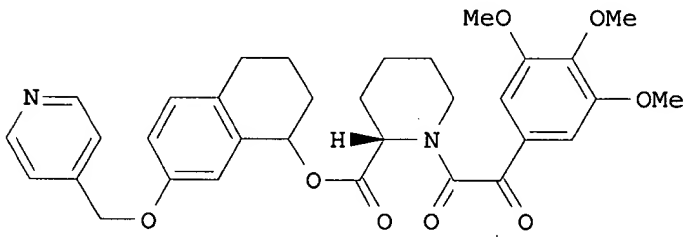
Absolute stereochemistry.



L8 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2002 ACS
AN 1998:338139 CAPLUS
DN 129:27894
TI Preparation of 1-tetralyl 1-oxoaracetylpiperidine-2-carboxylates and analogs as neurotrophic factor adjuncts
IN Zelle, Robert E.; Su, Michael
PA Vertex Pharmaceuticals Inc., USA
SO PCT Int. Appl., 50 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9820892	A1	19980522	WO 1997-US20867	19971113
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	US 5811434	A	19980922	US 1996-748448	19961113
	ZA 9710258	A	19980528	ZA 1997-10258	19971113
	AU 9854396	A1	19980603	AU 1998-54396	19971113
	EP 941112	A1	19990915	EP 1997-948308	19971113
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	CN 1239435	A	19991222	CN 1997-180249	19971113
	BR 9712947	A	20000328	BR 1997-12947	19971113
	JP 2001503777	T2	20010321	JP 1998-522866	19971113
PRAI	US 1996-748448	A	19961113		
	WO 1997-US20867	W	19971113		

OS MARPAT 129:27894
GI



I

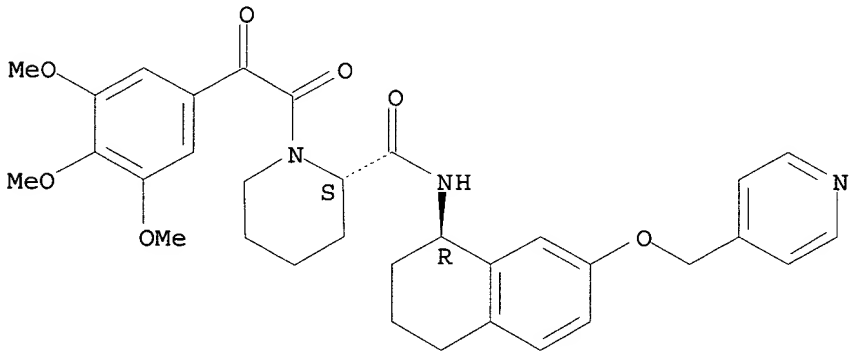
AB RZXCOCHR1NR2COCOR3 [R = (CH2)mAr or (CH2)mNR4R5; R1-R3 = alkyl or (hetero)aryl; R1R2 = atoms to complete a ring; R4,R5 = H, alkyl, (hetero)arylmethyl; NR4R5 = heterocyclyl; Ar = (hetero)aryl; Z = 5,6,7-(un)substituted 1,2,3,4-tetrahydro-1,2-naphthylene; m = 1-3] were prepd. as neurotrophic factor adjuncts for stimulation of neurite outgrowth (no data). Thus, 7-hydroxy-1-tetralone was etherified by 4-picolyl chloride and the reduced product esterified by (S)-1-allyloxycarbonylpiperidine-2-carboxylic acid to give, after deprotection, N-acylation, and resoln., title compds. (R)- and (S)-I.

IT **185143-87-7P 185143-95-7P 185143-97-9P 185144-17-6P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of 1-tetralyl 1-oxoaracetylpiperidine-2-carboxylates and analogs as neurotrophic factor adjuncts)

RN 185143-87-7 CAPLUS

CN 2-Piperidinecarboxamide, 1-[oxo(3,4,5-trimethoxyphenyl)acetyl]-N-[(1R)-1,2,3,4-tetrahydro-7-(4-pyridinylmethoxy)-1-naphthalenyl]-, (2S)- (9CI) (CA INDEX NAME)

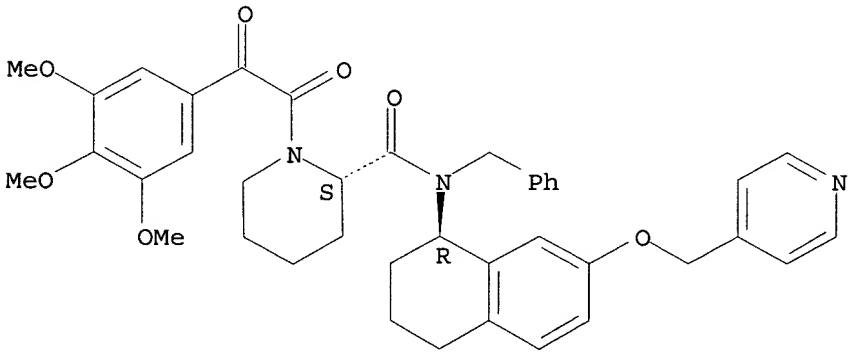
Absolute stereochemistry.



RN 185143-95-7 CAPLUS

CN 2-Piperidinecarboxamide, 1-[oxo(3,4,5-trimethoxyphenyl)acetyl]-N-(phenylmethyl)-N-[(1R)-1,2,3,4-tetrahydro-7-(4-pyridinylmethoxy)-1-naphthalenyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

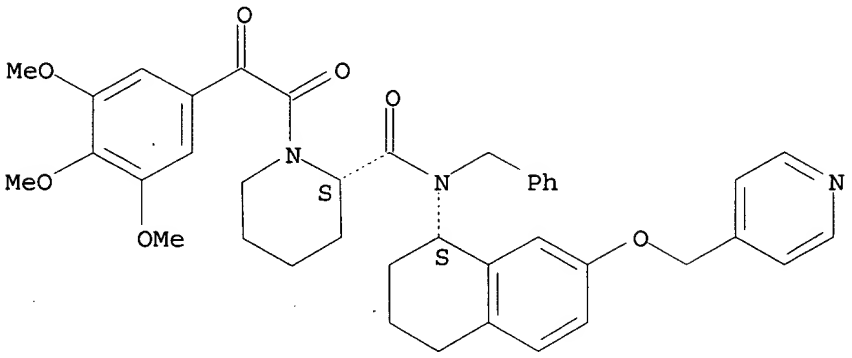


RN 185143-97-9 CAPLUS

CN 2-Piperidinecarboxamide, 1-[oxo(3,4,5-trimethoxyphenyl)acetyl]-N-

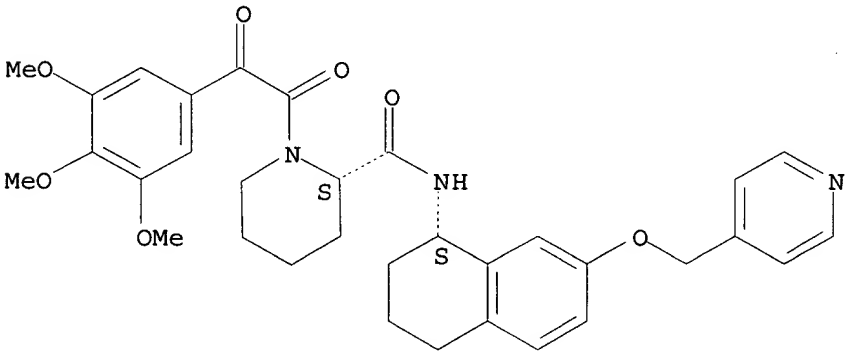
(phenylmethyl)-N-[(1S)-1,2,3,4-tetrahydro-7-(4-pyridinylmethoxy)-1-naphthalenyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 185144-17-6 CAPLUS
CN 2-Piperidinecarboxamide, 1-[oxo(3,4,5-trimethoxyphenyl)acetyl]-N-[(1S)-1,2,3,4-tetrahydro-7-(4-pyridinylmethoxy)-1-naphthalenyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2002 ACS
AN 1997:42010 CAPLUS
DN 126:74618
TI Preparation of tetralin compounds with mdr activity
IN Zelle, Robert E.
PA Vertex Pharmaceuticals Incorporated, USA
SO PCT Int. Appl., 50 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9636630	A1	19961121	WO 1996-US7094	19960516

W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI

RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML

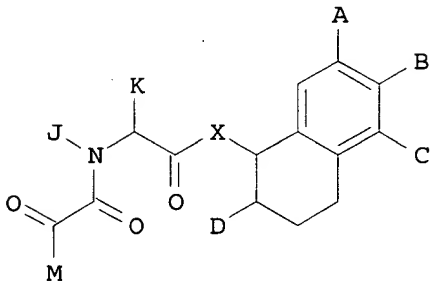
US	5726184	A	19980310	US 1995-444567	19950519
CA	2219752	AA	19961121	CA 1996-2219752	19960516
AU	9658620	A1	19961129	AU 1996-58620	19960516
AU	705167	B2	19990520		
EP	839143	A1	19980506	EP 1996-920255	19960516
EP	839143	B1	20020807		

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI

CN	1184475	A	19980610	CN 1996-194028	19960516
BR	9608789	A	19990217	BR 1996-8789	19960516
JP	11505255	T2	19990518	JP 1996-535063	19960516
AT	221881	E	20020815	AT 1996-920255	19960516
ZA	9603959	A	19961125	ZA 1996-3959	19960517
NO	9705198	A	19980119	NO 1997-5198	19971112
PRAI US	1995-444567	A	19950519		
	WO 1996-US7094	W	19960516		

OS MARPAT 126:74618

GI



I

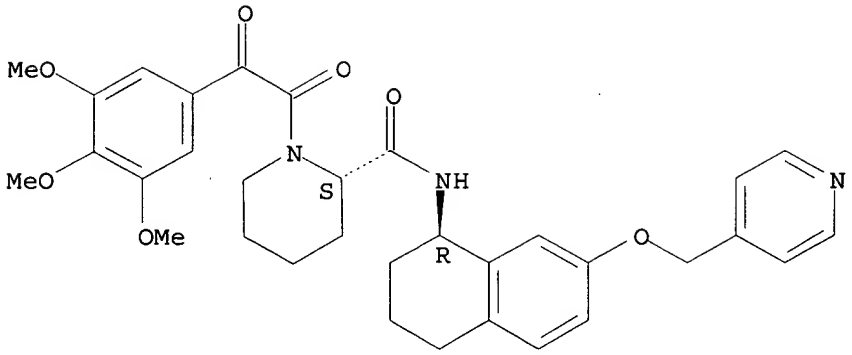
AB The present invention relates to compds. I that can maintain, increase or restore sensitivity of cells to therapeutic or prophylactic agents. I [A, B, C = H, halo, alkyl, alkoxy, (CH2)nAr, Y(CH2)nAr; Y = O, S, NR1 (R1 = alkyl, H); n = 0-4; Ar = carbocyclic or heterocyclic arom. group; D = H, (CH2)mE (E = Ar, NR4R5, R4 or R5 = H, alkyl, CH2Ar or R4R5 are a 5- or 6-membered heterocyclic ring; m = 1-3); X = O, NR6 (R6 = H, alkyl, (CH2)mAr); J, K = alkyl, alkyl-substituted Ar; JK = 5- or 6-membered ring; M = alkyl, Ar] were prepd. and multi-drug resistance assays conducted on the compds. E.g., 7-hydroxy-1-tetralone was treated with 4-picolyl chloride hydrochloride, reduced, resolved, reacted with alloc-(S)-pipecolic acid, and deprotected to give the 2-(7-pyridin-4-ylmethoxy)-1,2,3,4-tetrahydronaphthalen-1-yl ester of (S)-piperidine-2-carboxylic acid. The latter was treated with 3,4,5-trimethoxybenzoylformic acid to give the tetralin compd.

IT **185143-87-7P 185143-95-7P 185143-97-9P**
185144-17-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. and multi-drug resistance activity of tetralins)

RN 185143-87-7 CAPLUS

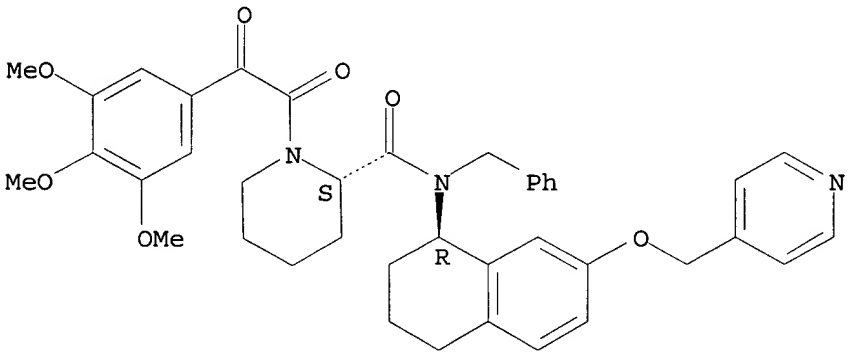
CN 2-Piperidinecarboxamide, 1-[oxo(3,4,5-trimethoxyphenyl)acetyl]-N-[(1R)-1,2,3,4-tetrahydro-7-(4-pyridinylmethoxy)-1-naphthalenyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



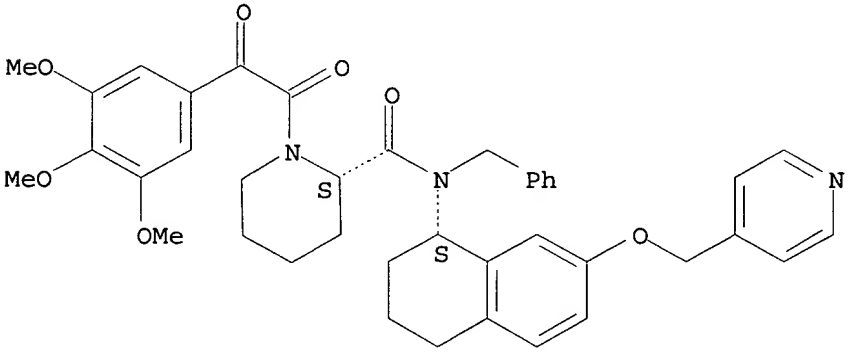
RN 185143-95-7 CAPLUS
CN 2-Piperidinecarboxamide, 1-[oxo(3,4,5-trimethoxyphenyl)acetyl]-N-(phenylmethyl)-N-[(1R)-1,2,3,4-tetrahydro-7-(4-pyridinylmethoxy)-1-naphthalenyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



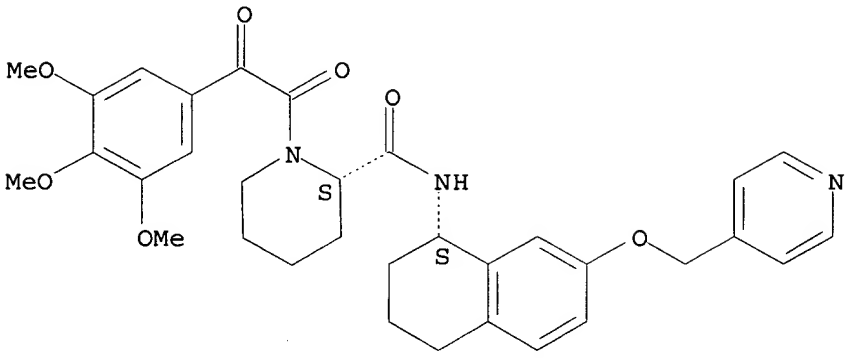
RN 185143-97-9 CAPLUS
CN 2-Piperidinecarboxamide, 1-[oxo(3,4,5-trimethoxyphenyl)acetyl]-N-(phenylmethyl)-N-[(1S)-1,2,3,4-tetrahydro-7-(4-pyridinylmethoxy)-1-naphthalenyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 185144-17-6 CAPLUS
CN 2-Piperidinecarboxamide, 1-[oxo(3,4,5-trimethoxyphenyl)acetyl]-N-[(1S)-1,2,3,4-tetrahydro-7-(4-pyridinylmethoxy)-1-naphthalenyl]-, (2S)- (9CI) (CA INDEX NAME)

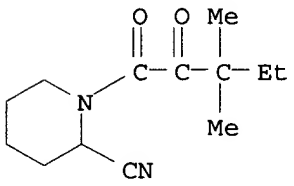
Absolute stereochemistry.



AN 1999:249062 CAPLUS
DN 130:262139
TI Method for treating hearing loss using sensorineurotrophic compounds
IN Magal, Ella
PA Amgen Inc., USA
SO PCT Int. Appl., 649 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 5

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9914998	A2	19990401	WO 1998-US19980	19980924
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	ZA 9808720	A	19990329	ZA 1998-8720	19980923
	CA 2304647	AA	19990401	CA 1998-2304647	19980924
	AU 9895783	A1	19990412	AU 1998-95783	19980924
	AU 742040	B2	20011213		
	EP 1011650	A1	20000628	EP 1998-949467	19980924
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	JP 2001516767	T2	20011002	JP 2000-512395	19980924
PRAI	US 1997-59905P	P	19970924		
	US 1997-59963P	P	19970925		
	US 1998-159105	A	19980923		
	WO 1998-US19980	W	19980924		

OS MARPAT 130:262139
AB Methods are provided for preventing and/or treating injury or degeneration of inner ear sensory cells, e.g. hair cells and auditory neurons, by administration of a sensorineurotrophic compd. to a patient in need thereof. Compd. prepn. is included.
IT **222171-50-8 222171-50-8D**, esters
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(sensorineurotrophic compds., and prepn. thereof, for treating hearing loss)
RN 222171-50-8 CAPLUS
CN 2-Piperidinecarbonitrile, 1-(3,3-dimethyl-1,2-dioxopentyl)- (9CI) (CA INDEX NAME)

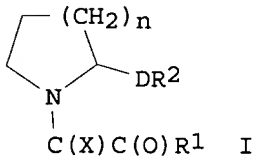


RN 222171-50-8 CAPLUS
CN 2-Piperidinecarbonitrile, 1-(3,3-dimethyl-1,2-dioxopentyl)- (9CI) (CA INDEX NAME)

AN 1999:784078 CAPLUS
DN 132:22860
TI Preparation of aza-heterocyclic compounds used to treat neurological disorders and hair loss
IN Hamilton, Gregory S.; Norman, Mark H.; Wu, Yong-Qian; Steiner, Joseph P.
PA Guilford Pharmaceuticals Inc., USA; Amgen, Inc.
SO PCT Int. Appl., 96 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 5

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9962881	A1	19991209	WO 1998-US25573	19981203
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	CA 2333963	AA	19991209	CA 1998-2333963	19981203
	AU 9917081	A1	19991220	AU 1999-17081	19981203
	ZA 9811063	A	20000707	ZA 1998-11063	19981203
	BR 9815920	A	20010220	BR 1998-15920	19981203
	EP 1084107	A1	20010321	EP 1998-961866	19981203
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	JP 2002516905	T2	20020611	JP 2000-552093	19981203
	NO 2000005903	A	20010202	NO 2000-5903	20001121
PRAI	US 1998-87788P	P	19980603		
	US 1998-101077P	P	19980918		
	WO 1998-US25573	W	19981203		

OS MARPAT 132:22860
GI



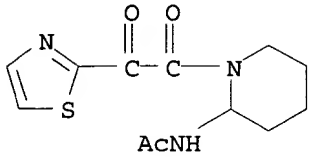
I

AB Prepn. of N-heterocyclic carboxylic acids and carboxylic acid isosteres I [n = 1-3; X = O, S; R1 = C1-C9 straight or branched chain alkyl, C2-C9 straight or branched chain alkenyl, aryl, heteroaryl, carboncycle, heterocycle; D = bond, C1-C10 straight or branched chain alkyl, C2-C10 alkenyl, C2-C10 alkynyl; R2 = carboxylic acid, carboxylic acid isostere] and their use for treating neurol. disorders and for treating alopecia and promoting hair growth are described. E.g., (2S)-1-(1,2-dioxo-3,3-dimethylpentyl)-2-hydroxymethylpyrrolidine was prepd.

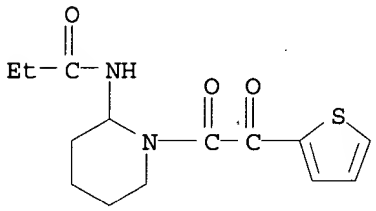
IT **251949-80-1P 251949-81-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of aza-heterocyclic compds. used to treat neurol. disorders and hair loss)

RN 251949-80-1 CAPLUS

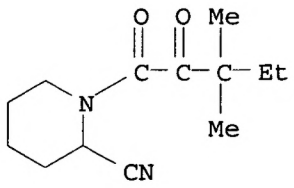
CN Acetamide, N-[1-(oxo-2-thiazolylacetyl)-2-piperidinyl]- (9CI) (CA INDEX NAME)



RN 251949-81-2 CAPLUS
CN Propanamide, N-[1-(oxo-2-thienylacetyl)-2-piperidinyl]- (9CI) (CA INDEX NAME)



RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT


O
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Me
CN

AN 1999:784078 CAPLUS
DN 132:22860
TI Preparation of aza-heterocyclic compounds used to treat neurological disorders and hair loss
IN Hamilton, Gregory S.; Norman, Mark H.; Wu, Yong-Qian; Steiner, Joseph P.
PA Guilford Pharmaceuticals Inc., USA; Amgen, Inc.
SO PCT Int. Appl., 96 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 5

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9962881	A1	19991209	WO 1998-US25573	19981203
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	CA 2333963	AA	19991209	CA 1998-2333963	19981203
	AU 9917081	A1	19991220	AU 1999-17081	19981203
	ZA 9811063	A	20000707	ZA 1998-11063	19981203
	BR 9815920	A	20010220	BR 1998-15920	19981203
	EP 1084107	A1	20010321	EP 1998-961866	19981203
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	JP 2002516905	T2	20020611	JP 2000-552093	19981203
	NO 2000005903	A	20010202	NO 2000-5903	20001121
PRAI	US 1998-87788P	P	19980603		
	US 1998-101077P	P	19980918		
	WO 1998-US25573	W	19981203		

OS MARPAT 132:22860
RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L42 ANSWER 9 OF 14 CAPLUS COPYRIGHT 2002 ACS

IT **222171-57-5P**

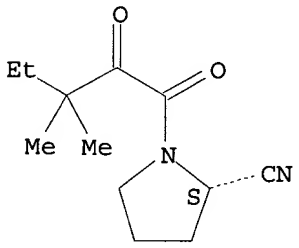
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(prepn. of aza-heterocyclic compds. used to treat neurol. disorders and hair loss)

RN 222171-57-5 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-(3,3-dimethyl-1,2-dioxopentyl)-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **251949-35-6P 251949-40-3P 251949-55-0P**
251949-59-4P 251949-60-7P 251949-61-8P
251949-62-9P 251949-63-0P 251949-91-4P
251949-92-5P 251949-94-7P 251949-95-8P
251950-09-1P 251950-10-4P 251950-43-3P

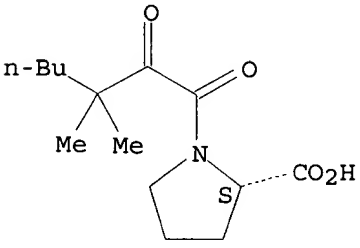
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of aza-heterocyclic compds. used to treat neurol. disorders and hair loss)

RN 251949-35-6 CAPLUS

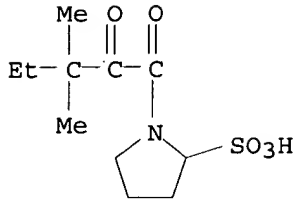
CN L-Proline, 1-(3,3-dimethyl-1,2-dioxoheptyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



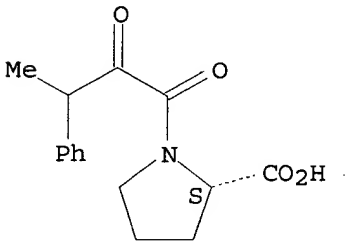
RN 251949-40-3 CAPLUS

CN 2-Pyrrolidinesulfonic acid, 1-(3,3-dimethyl-1,2-dioxopentyl)- (9CI) (CA INDEX NAME)

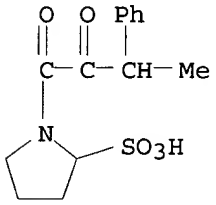


RN 251949-55-0 CAPLUS
CN L-Proline, 1-(1,2-dioxo-3-phenylbutyl)- (9CI) (CA INDEX NAME)

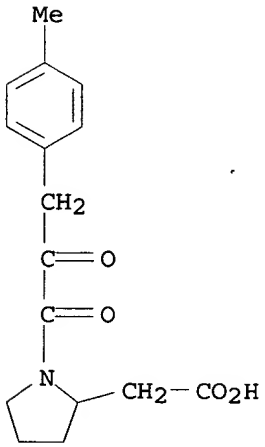
Absolute stereochemistry.



RN 251949-59-4 CAPLUS
CN 2-Pyrrolidinesulfonic acid, 1-(1,2-dioxo-3-phenylbutyl)- (9CI) (CA INDEX NAME)

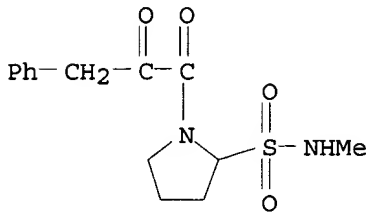


RN 251949-60-7 CAPLUS
CN 2-Pyrrolidineacetic acid, 1-[3-(4-methylphenyl)-1,2-dioxopropyl]- (9CI) (CA INDEX NAME)

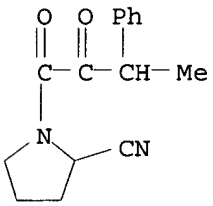


RN 251949-61-8 CAPLUS

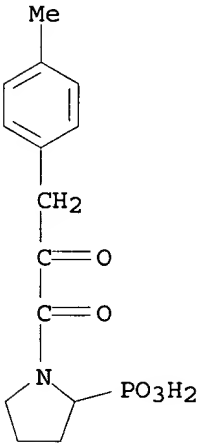
CN 2-Pyrrolidinesulfonamide, 1-(1,2-dioxo-3-phenylpropyl)-N-methyl- (9CI) (CA INDEX NAME)



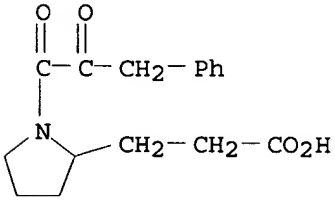
RN 251949-62-9 CAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-(1,2-dioxo-3-phenylbutyl)- (9CI) (CA INDEX NAME)

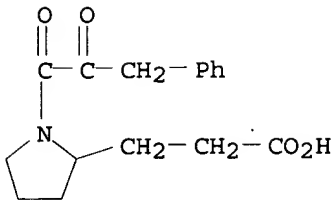


RN 251949-63-0 CAPLUS
CN Phosphonic acid, [1-[3-(4-methylphenyl)-1,2-dioxopropyl]-2-pyrrolidinyl]- (9CI) (CA INDEX NAME)



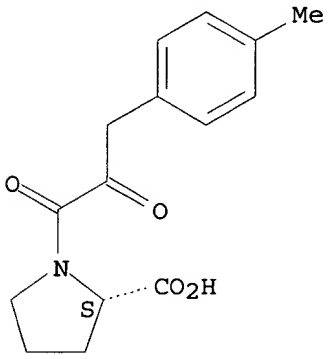
RN 251949-91-4 CAPLUS
CN 2-Pyrrolidinepropanoic acid, 1-(1,2-dioxo-3-phenylpropyl)- (9CI) (CA INDEX NAME)



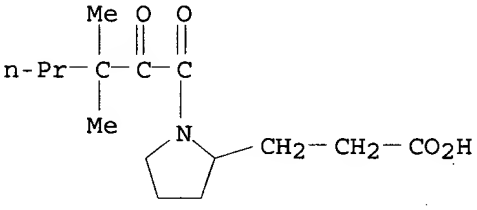


RN 251949-92-5 CAPLUS
CN L-Proline, 1-[3-(4-methylphenyl)-1,2-dioxopropyl]- (9CI) (CA INDEX NAME)

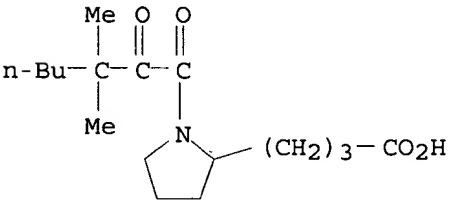
Absolute stereochemistry.



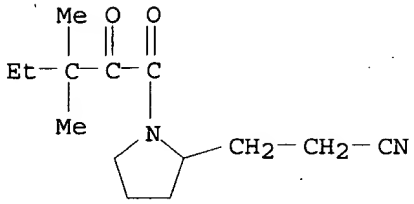
RN 251949-94-7 CAPLUS
CN 2-Pyrrolidinepropanoic acid, 1-(3,3-dimethyl-1,2-dioxohexyl)- (9CI) (CA INDEX NAME)



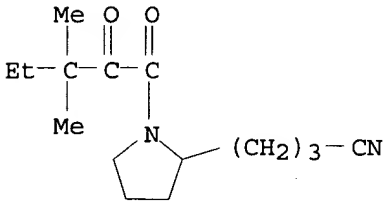
RN 251949-95-8 CAPLUS
CN 2-Pyrrolidinebutanoic acid, 1-(3,3-dimethyl-1,2-dioxoheptyl)- (9CI) (CA INDEX NAME)



RN 251950-09-1 CAPLUS
CN 2-Pyrrolidinepropanenitrile, 1-(3,3-dimethyl-1,2-dioxopentyl)- (9CI) (CA INDEX NAME)

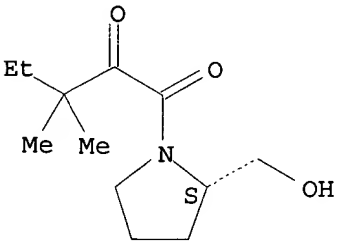


RN 251950-10-4 CAPLUS
CN 2-Pyrrolidinebutanenitrile, 1-(3,3-dimethyl-1,2-dioxopentyl)- (9CI) (CA INDEX NAME)



RN 251950-43-3 CAPLUS
CN 2-Pyrrolidinemethanol, 1-(3,3-dimethyl-1,2-dioxopentyl)-, (2S)- (9CI) (CA INDEX NAME)

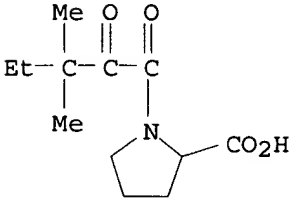
Absolute stereochemistry.



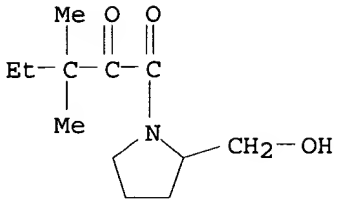
AN 1999:784077 CAPLUS
DN 132:18813
TI N-linked sulfonamides of N-heterocyclic carboxylic acids or carboxylic acid isosteres for treatment of neurological disorders and alopecia
IN Hamilton, Gregory S.; Norman, Mark H.; Wu, Yong-Qian
PA Guilford Pharmaceuticals Inc., USA; Amgen, Inc.
SO PCT Int. Appl., 96 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9962880	A1	19991209	WO 1998-US25572	19981203
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	ZA 9811060	A	19991203	ZA 1998-11060	19981203
	CA 2334002	AA	19991209	CA 1998-2334002	19981203
	AU 9917080	A1	19991220	AU 1999-17080	19981203
	EP 1084106	A1	20010321	EP 1998-961865	19981203
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	JP 2002516904	T2	20020611	JP 2000-552092	19981203
	BR 9815882	A	20020917	BR 1998-15882	19981203
	NO 2000006078	A	20010205	NO 2000-6078	20001130
PRAI	US 1998-87842P	P	19980603		
	WO 1998-US25572	W	19981203		

OS MARPAT 132:18813
AB The invention relates to N-linked sulfonamides of N-heterocyclic carboxylic acid and carboxylic acid isosteres, their prepn., and use for treating neurol. disorders, including phys. damaged nerves and neurodegenerative diseases, and for treating alopecia and promoting hair growth.
IT **251917-38-1 251917-39-2**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(N-linked sulfonamides of N-heterocyclic carboxylic acids or carboxylic acid isosteres for treatment of neurol. disorders and alopecia)
RN 251917-38-1 CAPLUS
CN Proline, 1-(3,3-dimethyl-1,2-dioxopentyl)- (9CI) (CA INDEX NAME)



RN 251917-39-2 CAPLUS
CN 2-Pyrrolidinemethanol, 1-(3,3-dimethyl-1,2-dioxopentyl)- (9CI) (CA INDEX NAME)

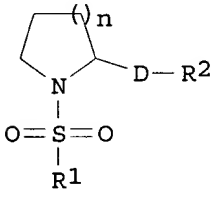


RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

AN 2002:332702 CAPLUS
DN 136:355153
TI Preparation of pyrrolidino and piperidino sulfonamides for treatment of neurological disorders and alopecia
IN Hamilton, Gregory S.; Norman, Mark H.; Wu, Yong-qian
PA USA
SO U.S. Pat. Appl. Publ., 29 pp., Cont.-in-part of U. S. Provisional Ser. No. 87,842.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2002052510	A1	20020502	US 1998-204236	19981203
	ZA 9811060	A	19991203	ZA 1998-11060	19981203
	US 2002052514	A1	20020502	US 2001-791660	20010226
PRAI	US 1998-87842P	P	19980603		
	US 1998-204236	A3	19981203		

OS MARPAT 136:355153
GI



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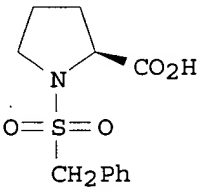
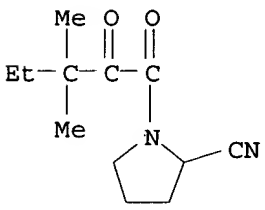


II

AB Title compds. I [R1 = H, alkyl, alkenyl, aryl, heteroaryl, carbocycle, heterocycle; D = bond, alk(en/yn)yl; R2 = carboxylic acid, (un)substituted carboxylic acid isostere; n = 1-2, with some provisions] were prepd. For instance, proline Me ester hydrochloride salt was converted to the N-benzylsulfonyl deriv. (CH2Cl2, Et3N, PhCH2SO2Cl, 0.degree.C) and sapond. (MeOH, LiOH)to give II. In an MPTP model of Parkinson's disease in mice, II at 4 mg/kg caused a 24.4% recovery of dopaminergic neurons. I are useful in the treatment of Alzheimer's disease, Parkinson's disease, amyotrophic lateral sclerosis and hair loss.

IT **251917-41-6**, 2-Pyrrolidinecarbonitrile, 1-(3,3-dimethyl-1,2-dioxopentyl)-
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prepn. of pyrrolidino and piperidino sulfonamides for treatment of neurol. disorders and alopecia)

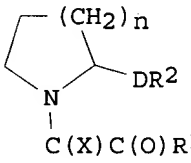
RN 251917-41-6 CAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-(3,3-dimethyl-1,2-dioxopentyl)- (9CI) (CA INDEX NAME)



AN 1999:784078 CAPLUS
DN 132:22860
TI Preparation of aza-heterocyclic compounds used to treat neurological disorders and hair loss
IN Hamilton, Gregory S.; Norman, Mark H.; Wu, Yong-Qian; Steiner, Joseph P.
PA Guilford Pharmaceuticals Inc., USA; Amgen, Inc.
SO PCT Int. Appl., 96 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 5

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9962881	A1	19991209	WO 1998-US25573	19981203
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	CA 2333963	AA	19991209	CA 1998-2333963	19981203
	AU 9917081	A1	19991220	AU 1999-17081	19981203
	ZA 9811063	A	20000707	ZA 1998-11063	19981203
	BR 9815920	A	20010220	BR 1998-15920	19981203
	EP 1084107	A1	20010321	EP 1998-961866	19981203
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	JP 2002516905	T2	20020611	JP 2000-552093	19981203
	NO 2000005903	A	20010202	NO 2000-5903	20001121
PRAI	US 1998-87788P	P	19980603		
	US 1998-101077P	P	19980918		
	WO 1998-US25573	W	19981203		

OS MARPAT 132:22860
GI



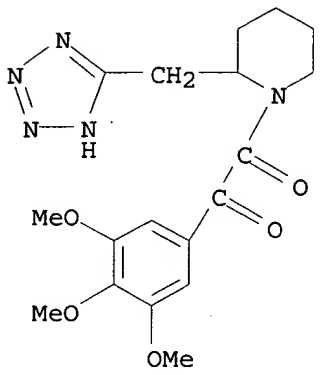
I

AB Prepn. of N-heterocyclic carboxylic acids and carboxylic acid isosteres I [n = 1-3; X = O, S; R1 = C1-C9 straight or branched chain alkyl, C2-C9 straight or branched chain alkenyl, aryl, heteroaryl, carboncycle, heterocycle; D = bond, C1-C10 straight or branched chain alkyl, C2-C10 alkenyl, C2-C10 alkynyl; R2 = carboxylic acid, carboxylic acid isostere] and their use for treating neurol. disorders and for treating alopecia and promoting hair growth are described. E.g., (2S)-1-(1,2-dioxo-3,3-dimethylpentyl)-2-hydroxymethylpyrrolidine was prepd.

IT **251949-52-7P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of aza-heterocyclic compds. used to treat neurol. disorders and hair loss)

RN 251949-52-7 CAPLUS

CN Piperidine, 1-[oxo(3,4,5-trimethoxyphenyl)acetyl]-2-(1H-tetrazol-5-ylmethyl)- (9CI) (CA INDEX NAME)

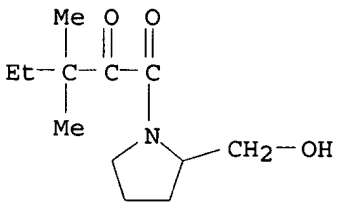


RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

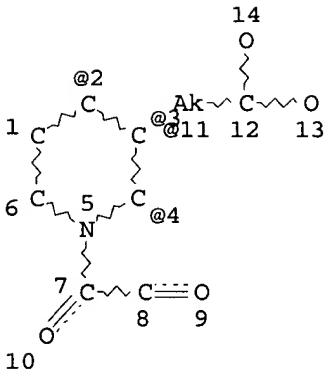
AN 1999:784077 CAPLUS
DN 132:18813
TI N-linked sulfonamides of N-heterocyclic carboxylic acids or carboxylic acid isosteres for treatment of neurological disorders and alopecia
IN Hamilton, Gregory S.; Norman, Mark H.; Wu, Yong-Qian
PA Guilford Pharmaceuticals Inc., USA; Amgen, Inc.
SO PCT Int. Appl., 96 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9962880	A1	19991209	WO 1998-US25572	19981203
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	ZA 9811060	A	19991203	ZA 1998-11060	19981203
	CA 2334002	AA	19991209	CA 1998-2334002	19981203
	AU 9917080	A1	19991220	AU 1999-17080	19981203
	EP 1084106	A1	20010321	EP 1998-961865	19981203
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	JP 2002516904	T2	20020611	JP 2000-552092	19981203
	BR 9815882	A	20020917	BR 1998-15882	19981203
	NO 2000006078	A	20010205	NO 2000-6078	20001130
PRAI	US 1998-87842P	P	19980603		
	WO 1998-US25572	W	19981203		

OS MARPAT 132:18813
AB The invention relates to N-linked sulfonamides of N-heterocyclic carboxylic acid and carboxylic acid isosteres, their prepn., and use for treating neurol. disorders, including phys. damaged nerves and neurodegenerative diseases, and for treating alopecia and promoting hair growth.
IT **251917-39-2**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(N-linked sulfonamides of N-heterocyclic carboxylic acids or carboxylic acid isosteres for treatment of neurol. disorders and alopecia)
RN 251917-39-2 CAPLUS
CN 2-Pyrrolidinemethanol, 1-(3,3-dimethyl-1,2-dioxopentyl)- (9CI) (CA INDEX NAME)



RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

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SAMPLE SCREEN SEARCH COMPLETED -   2626 TO ITERATE

 38.1% PROCESSED    1000 ITERATIONS                                  0 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.02

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:        49448 TO    55592
PROJECTED ANSWERS:               0 TO        0

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FULL SCREEN SEARCH COMPLETED -  52020 TO ITERATE

100.0% PROCESSED   52020 ITERATIONS                                16 ANSWERS
SEARCH TIME: 00.00.03

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L11           8 L10

=> d bib abs hitstr 1-8

L11  ANSWER 1 OF 8  CAPLUS  COPYRIGHT 2002 ACS
AN   2002:271982  CAPLUS
DN   136:294967
TI   Preparation of solenopsin derivatives and analogues as fire ant
     suppressants
IN   Bowen, J. Phillip; Furness, M. Scott; Whitmire, David
PA   USA
SO   U.S., 24 pp.
     CODEN: USXXAM
DT   Patent
LA   English
FAN.CNT 1
     PATENT NO.         KIND  DATE          APPLICATION NO.  DATE
     ---------------    ----  --------      ---------------  --------
PI   US 6369078          B1   20020409      US 2000-650257   20000829
PRAI US 1999-151724P     P    19990831
OS   MARPAT 136:294967
GI
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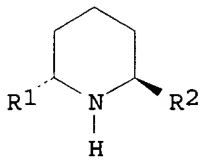

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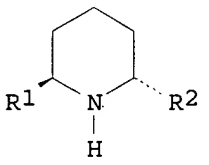


II

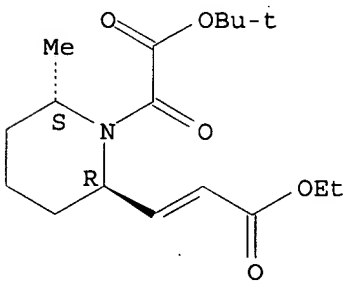
AB Solenopsin alkaloid derivs., such as I or II [R1 = C1 to C20 (un)satd., linear, cyclic or branch-chained (un)substituted alkyl; (un)substituted arom., ester], and salts thereof, were prepd. for their use as inhibitors of the biosynthesis of the venom of fire ants and/or insecticides. Thus, solenopsin hydrochloride II [R1 = Me, R2 = (CH2)10Me].HCl was prepd. via a multistep synthetic sequence starting from 1-bromoundecane, 4-chloropyridine hydrochloride and iodomethane.

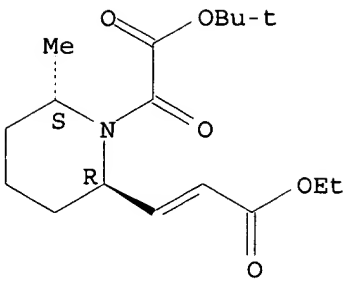
IT **409061-35-4P 409061-36-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of solenopsin derivs. and analogs as fire ant suppressants)

RN 409061-35-4 CAPLUS

CN 1-Piperidineacetic acid, 2-(3-ethoxy-3-oxo-1-propenyl)-6-methyl-.alpha.-oxo-, 1,1-dimethylethyl ester, (2R,6S)-rel- (9CI) (CA INDEX NAME)

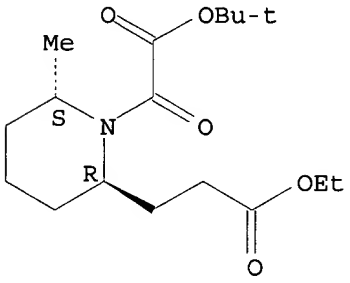
Relative stereochemistry.
Double bond geometry unknown.





RN 409061-36-5 CAPLUS
CN 2-Piperidinepropanoic acid, 1-[(1,1-dimethylethoxy)oxoacetyl]-6-methyl-, ethyl ester, (2R,6S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RE.CNT 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 2 OF 8 CAPLUS COPYRIGHT 2002 ACS
AN 2001:916406 CAPLUS
DN 136:31715
TI Carboxylic acids and carboxylic acid isosteres of N-heterocyclic compounds, preparation thereof, and use in the treatment of neurological and other disorders
IN Hamilton, Gregory S.; Norman, Mark H.; Wu, Yong-Qian
PA GPI Nil Holdings, Inc., USA
SO U.S., 62 pp., Cont.-in-part of U.S. Ser. No. 204,237, abandoned.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 5

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6331537	B1	20011218	US 1999-453571	19991202
	ZA 9811063	A	20000707	ZA 1998-11063	19981203
	WO 2000032588	A2	20000608	WO 1999-US28663	19991203
	WO 2000032588	A3	20010222		
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	BR 9916461	A	20010904	BR 1999-16461	19991203
	EP 1135370	A2	20010926	EP 1999-961930	19991203

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO

NO 2001002765 A 20010720 NO 2001-2765 20010605

PRAI US 1998-87788P P 19980603
US 1998-204237 B2 19981203
US 1999-453571 A 19991202
WO 1999-US28663 W 19991203

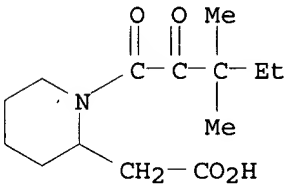
OS MARPAT 136:31715

AB N-heterocyclic carboxylic acids and carboxylic acid isosteres are provided, as are their prepn. and their use for treating neurol. disorders including phys. damaged nerves and neurodegenerative diseases, for treating alopecia and promoting hair growth, for treating vision disorders and/or improving vision, and for treating memory impairment and/or enhancing memory performance by administering such compds.

IT **273924-91-7P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(carboxylic acids and carboxylic acid isosteres of N-heterocyclic compds., prepn., and use in treatment of neurol. and other disorders)

RN 273924-91-7 CAPLUS

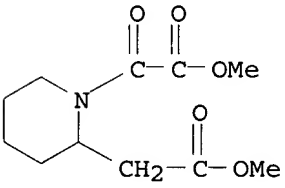
CN 2-Piperidineacetic acid, 1-(3,3-dimethyl-1,2-dioxopentyl)- (9CI) (CA INDEX NAME)



IT **115909-55-2P 380344-15-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and reaction; carboxylic acids and carboxylic acid isosteres of N-heterocyclic compds., prepn., and use in treatment of neurol. and other disorders)

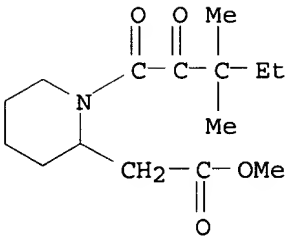
RN 115909-55-2 CAPLUS

CN 1,2-Piperidinediacetic acid, .alpha.1-oxo-, dimethyl ester (9CI) (CA INDEX NAME)



RN 380344-15-0 CAPLUS

CN 2-Piperidineacetic acid, 1-(3,3-dimethyl-1,2-dioxopentyl)-, methyl ester (9CI) (CA INDEX NAME)

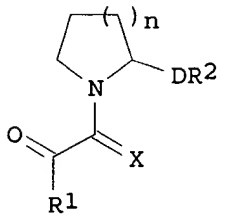


RE.CNT 364 THERE ARE 364 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 3 OF 8 CAPLUS COPYRIGHT 2002 ACS
AN 2000:384175 CAPLUS
DN 133:30959
TI Preparation of prolinylalkanediones and related compounds for treating neurological disease, vision disorders, and alopecia.
IN Hamilton, Gregory S.; Norman, Mark H.; Wu, Yong-qian
PA GPI Nil Holdings, Inc., USA; Amgen, Inc.
SO PCT Int. Appl., 166 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 5

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000032588	A2	20000608	WO 1999-US28663	19991203
	WO 2000032588	A3	20010222		
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	US 6331537	B1	20011218	US 1999-453571	19991202
	BR 9916461	A	20010904	BR 1999-16461	19991203
	EP 1135370	A2	20010926	EP 1999-961930	19991203
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	NO 2001002765	A	20010720	NO 2001-2765	20010605
PRAI	US 1998-204237	A	19981203		
	US 1999-453571	A	19991202		
	US 1998-87788P	P	19980603		
	WO 1999-US28663	W	19991203		

OS MARPAT 133:30959
GI



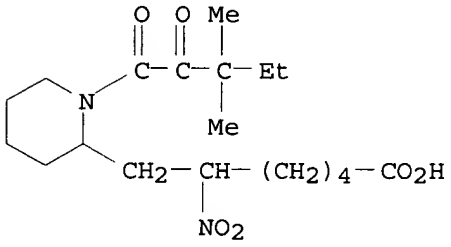
I

AB Title compds. [I; n = 1-3; X = O, S; R1 = (substituted) alkyl, alkenyl, aryl, heteroaryl, carbocyclyl, heterocyclyl; D = bond, (substituted) alkyl, alkenyl, alkynyl; R2 = CO2H, (substituted) CO2H isostere], were prepd. Thus, L-proline Me ester hydrochloride in CH2Cl2 was treated with Et3N and then with MeO2CCOCl to give 88% Me (2S)-1-(1,2-dioxo-2-methoxyethyl)-2-pyrrolidinecarboxylate. The latter in THF at -78.degree. was treated with 1,1-dimethylpropylmagnesium chloride followed by 3 h stirring at -78.degree. to give 75% Me (2S)-1-(1,2-dioxo-3,3-dimethylpentyl)-2-pyrrolidinecarboxylate. This was stirred overnight with aq. LiOH in MeOH to give 87% (2S)-1-(1,2-dioxo-3,3-dimethylpentyl)-2-pyrrolidinecarboxylic acid. In the MPTP model of Parkinson's disease in mice, I at 10 mg/kg orally gave 10.4-46.5% recovery of TH-stained dopaminergic neurons.

IT **251950-08-0P 273924-91-7P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of prolinylalkanediones and related compds. for treating neurol. disease, vision disorders, and alopecia)

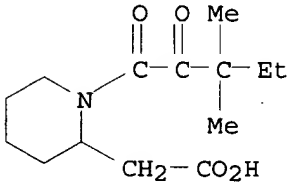
RN 251950-08-0 CAPLUS

CN 2-Piperidineheptanoic acid, 1-(3,3-dimethyl-1,2-dioxopentyl)-.epsilon.-nitro- (9CI) (CA INDEX NAME)



RN 273924-91-7 CAPLUS

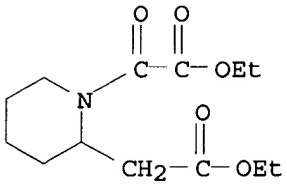
CN 2-Piperidineacetic acid, 1-(3,3-dimethyl-1,2-dioxopentyl)- (9CI) (CA INDEX NAME)



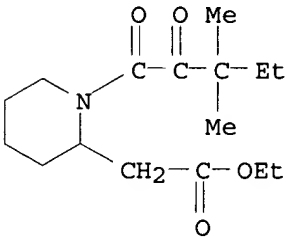
IT **273925-03-4P 273925-04-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of prolinylalkanediones and related compds. for treating neurol. disease, vision disorders, and alopecia)

RN 273925-03-4 CAPLUS

CN 1,2-Piperidinediacetic acid, .alpha.-oxo-, diethyl ester (9CI) (CA INDEX NAME)



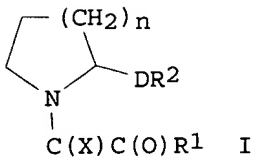
RN 273925-04-5 CAPLUS
CN 2-Piperidineacetic acid, 1-(3,3-dimethyl-1,2-dioxopentyl)-, ethyl ester (9CI) (CA INDEX NAME)



L11 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2002 ACS
AN 1999:784078 CAPLUS
DN 132:22860
TI Preparation of aza-heterocyclic compounds used to treat neurological disorders and hair loss
IN Hamilton, Gregory S.; Norman, Mark H.; Wu, Yong-Qian; Steiner, Joseph P.
PA Guilford Pharmaceuticals Inc., USA; Amgen, Inc.
SO PCT Int. Appl., 96 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 5

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9962881	A1	19991209	WO 1998-US25573	19981203
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	CA 2333963	AA	19991209	CA 1998-2333963	19981203
	AU 9917081	A1	19991220	AU 1999-17081	19981203
	ZA 9811063	A	20000707	ZA 1998-11063	19981203
	BR 9815920	A	20010220	BR 1998-15920	19981203
	EP 1084107	A1	20010321	EP 1998-961866	19981203
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	JP 2002516905	T2	20020611	JP 2000-552093	19981203
	NO 2000005903	A	20010202	NO 2000-5903	20001121
PRAI	US 1998-87788P	P	19980603		
	US 1998-101077P	P	19980918		
	WO 1998-US25573	W	19981203		

OS MARPAT 132:22860
GI

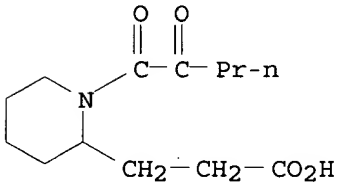


I

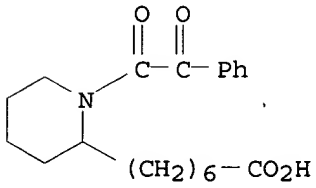
AB Prepn. of N-heterocyclic carboxylic acids and carboxylic acid isosteres I [n = 1-3; X = O, S; R1 = C1-C9 straight or branched chain alkyl, C2-C9 straight or branched chain alkenyl, aryl, heteroaryl, carboncycle, heterocycle; D = bond, C1-C10 straight or branched chain alkyl, C2-C10 alkenyl, C2-C10 alkynyl; R2 = carboxylic acid, carboxylic acid isostere] and their use for treating neurol. disorders and for treating alopecia and promoting hair growth are described. E.g., (2S)-1-(1,2-dioxo-3,3-dimethylpentyl)-2-hydroxymethylpyrrolidine was prepd.

IT **251949-46-9P 251949-50-5P 251949-51-6P 251950-08-0P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of aza-heterocyclic compds. used to treat neurol. disorders and hair loss)

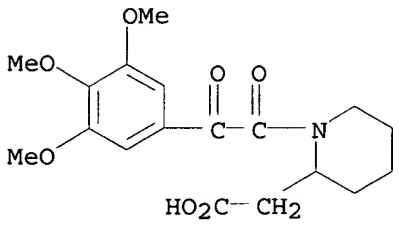
RN 251949-46-9 CAPLUS
CN 2-Piperidinepropanoic acid, 1-(1,2-dioxopentyl)- (9CI) (CA INDEX NAME)



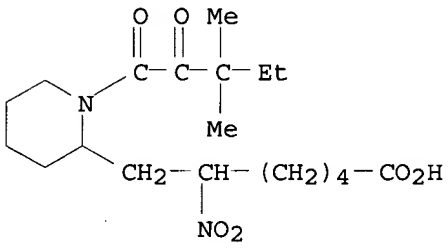
RN 251949-50-5 CAPLUS
CN 2-Piperidineheptanoic acid, 1-(oxophenylacetyl)- (9CI) (CA INDEX NAME)



RN 251949-51-6 CAPLUS
CN 2-Piperidineacetic acid, 1-[oxo(3,4,5-trimethoxyphenyl)acetyl]- (9CI) (CA INDEX NAME)



RN 251950-08-0 CAPLUS
CN 2-Piperidineheptanoic acid, 1-(3,3-dimethyl-1,2-dioxopentyl)-.epsilon.-nitro- (9CI) (CA INDEX NAME)

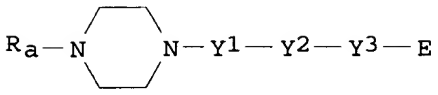


RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2002 ACS
AN 1996:483488 CAPLUS
DN 125:142582
TI Piperazine derivatives: medicaments containing them, their use, and processes for their preparation
IN Pieper, Helmut; Austel, Volkhard; Himmelsbach, Frank; Linz, Guenther; Guth, Brian; Weisenberger, Johannes
PA Thomae, Dr. Karl, G.m.b.H., Germany
SO Eur. Pat. Appl., 45 pp.
CODEN: EPXXDW
DT Patent
LA German
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 718287	A2	19960626	EP 1995-120118	19951219
	EP 718287	A3	19970129		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	DE 4446300	A1	19960627	DE 1994-4446300	19941223
	DE 19533224	A1	19970313	DE 1995-19533224	19950908
	US 5700801	A	19971223	US 1995-572256	19951213
	AU 9540558	A1	19960704	AU 1995-40558	19951219
	CA 2165922	AA	19960624	CA 1995-2165922	19951221
	BR 9505981	A	19971223	BR 1995-5981	19951221
	CN 1131665	A	19960925	CN 1995-121745	19951223
	JP 08231509	A2	19960910	JP 1995-336774	19951225
PRAI	DE 1994-4446300		19941223		
	DE 1995-19533224		19950908		

OS CASREACT 125:142582; MARPAT 125:142582
GI

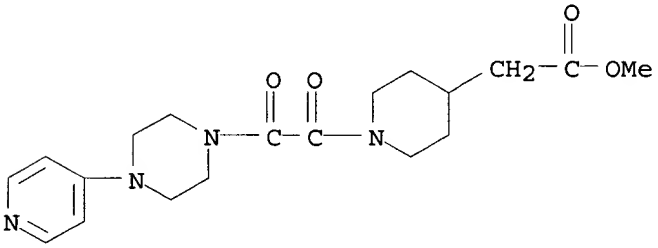


I

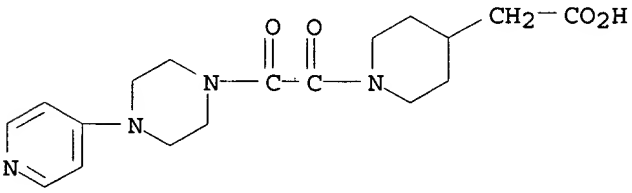
AB The prepn. of title compds. I [Ra = substituted pyridyl group; Y1 = CO, COCO, substituted CO, (un)substituted SO2, aminocarbonyl, etc.; Y2 = (un)substituted 1,3- or 1,4-phenylene, 3- or 4-piperidinyl, etc.; Y3 = CH2CO, CH2CH2CO, OCH2CO, etc.; E = OH, OMe, OEt, Me3CO, etc.], useful as antithrombotics and blood platelet aggregation inhibitor, is described. Thus, condensation of 1-(4-pyridyl)piperazine with Me acrylate in the presence of methanolic soln. of benzyltrimethylammonium hydroxide in CHCl3 followed by LiOH hydrolysis gave 3-[4-(4-pyridyl)piperazin-1-yl]propionic acid which on treatment with Me p-trans-aminocyclohexanecarboxylate hydrochloride in the presence of 2-(1H-benzotriazol-1-yl)-1,1,3,3-tetramethyluronium tetrafluoroborate-1-hydroxy-1H-benzotriazole-N-methylmorpholine in DMF gave title compd., Me [4-trans-[3-[4-(4-pyridyl)piperazin-1-yl]propionyl]amino]cyclohexanecarboxylate. Antithrombotic and blood platelet aggregation inhibitor activity of some of the compds. prepd. is given.

IT **179689-63-5P 179690-15-4P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of piperazine derivs. as antithrombotics and blood platelet aggregation inhibitor)

RN 179689-63-5 CAPLUS
CN 4-Piperidineacetic acid, 1-[oxo[4-(4-pyridinyl)-1-piperazinyl]acetyl]-, methyl ester (9CI) (CA INDEX NAME)

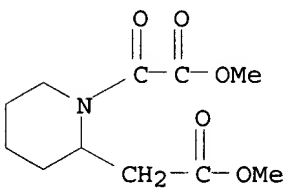


RN 179690-15-4 CAPLUS
CN 4-Piperidineacetic acid, 1-[oxo[4-(4-pyridinyl)-1-piperazinyl]acetyl]- (9CI) (CA INDEX NAME)

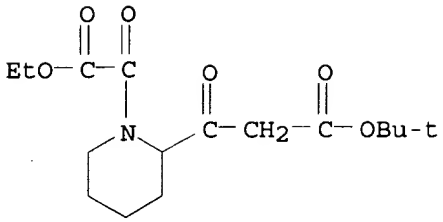


L11 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2002 ACS
AN 1988:492914 CAPLUS
DN 109:92914
TI Synthesis of deuterium labelled thioridazine via ruthenium tetroxide

oxidation of the piperidine ring
AU Mohammad, T.; Midha, K. K.; Hawes, E. M.
CS Coll. Pharm., Univ. Saskatchewan, Saskatoon, SK, S7N 0W0, Can.
SO Journal of Labelled Compounds and Radiopharmaceuticals (1988), 25(4), 415-27
CODEN: JLCRD4; ISSN: 0362-4803
DT Journal
LA English
OS CASREACT 109:92914
AB A multistep synthetic route to (.+-.)-10-[2-(1-methyl-2-piperidinyl)ethyl]-2-methylthio-10H-phenothiazine(thioridazine) was developed which allowed for the incorporation of two deuterium atoms in the piperidine ring and a further two in the 1-position of the Et side chain. The key steps involved ruthenium tetroxide oxidn. of N-protected Me 2-piperidinylacetate and subsequent LiAlD4 redn. of 2-(2-hydroxyethyl)-1-methyl-6-piperidinone or the corresponding piperidino ester. The isotopic purity of the dideuterated and tetradeuterated products was greater than 99%.
IT **115909-55-2P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 115909-55-2 CAPLUS
CN 1,2-Piperidinediacetic acid, .alpha.1-oxo-, dimethyl ester (9CI) (CA INDEX NAME)



L11 ANSWER 7 OF 8 CAPLUS COPYRIGHT 2002 ACS
AN 1978:528811 CAPLUS
DN 89:128811
TI Periodate oxidation of .alpha.-keto .gamma.-lactams. Enol oxidation and .beta.-lactam formation. Mechanism of periodate hydroxylation reactions
AU Bender, Dean R.; Brennan, John; Rapoport, Henry
CS Dep. Chem., Univ. California, Berkeley, Calif., USA
SO J. Org. Chem. (1978), 43(17), 3354-62
CODEN: JOCEAH; ISSN: 0022-3263
DT Journal
LA English
AB Periodate oxidn. of .alpha.-keto .gamma.-lactams results in .beta.-lactam formation (by oxidative ring contraction) and in 2 modes of enol oxidn. The relative rates of these oxidn. paths are related to electron distribution over the 3-atom portion comprising the .alpha.-keto group and the .beta. C, as demonstrated by the dependence of oxidn. rate and product distribution on the electronic properties of the .beta. substituent. Depending on the .beta.-substituent, some .alpha.-keto .gamma.-lactams are also oxidized by iodate. The 2 modes of enol oxidn. and the factors detg. which mode predominates appear to provide a unified mechanistic interpretation for periodate hydroxylation reactions in general.
IT **66552-07-6P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 66552-07-6 CAPLUS
CN 2-Piperidinepropanoic acid, 1-(ethoxyoxoacetyl)-.beta.-oxo-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



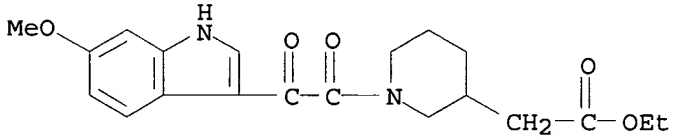
L11 ANSWER 8 OF 8 CAPLUS COPYRIGHT 2002 ACS
AN 1964:38952 CAPLUS
DN 60:38952
OREF 60:6898a-h,6899a-b
TI Synthesis of an analog of reserpine: O-(3,4,5-trimethoxybenzoate) of 3-[2-[3-(2-hydroxyethyl)piperidinolethyl]-6-methoxyindole
AU Najer, Henry; Giudicelli, Rene; Loiseau, Jacques; Menin, Jacques
CS Lab. Dausse, Paris
SO Bull. Soc. Chim. France (1963), (12), 2831-40
DT Journal
LA Unavailable
GI For diagram(s), see printed CA Issue.
AB NaOH (2N, 535 cc.) added to a soln. of 78.7 g. K salt of Et (2-nitro-4-methoxyphenyl)pyruvate (I) in 1600 cc. alc., and the soln. allowed to stand 1.5 hrs. at room temp. gave 39.5% (2-nitro-4-methoxyphenyl)pyruvic acid (II), m. 138-42.degree. (Kofler block), m. 179-80.degree. (Maquenne block). I (95 g.), 1280 cc. alc., 1026 cc. glacial HOAc, and 247 g. powd. Fe heated 15 min. to 75.degree. (when an exothermic reaction began), and the stirred mixt. kept 20 min. at 75.degree. gave 78% 2-carbethoxy-6-methoxyindole (IIa), m. 135-6.degree.. Similarly, II gave 83% 2-carboxy-6-methoxyindole (III), m. 199-200.degree.. Sapon. of IIa gave 97% III. III NH4 salt (10 g.) in 40 cc. glycerol heated 10 min. at 210-20.degree. gave 55% 6-methoxyindole (IV), m. 91.degree.. Pyruvic acid (20.5 g.) in 500 cc. H2O added to a soln. of 32.5 g. (3-methoxyphenyl)hydrazine in 325 cc. H2O and 32.5 cc. HOAc gave 93.5% pyruvic acid (3-methoxyphenyl)hydrazone, m. 118-19.degree. (50% alc.). A soln. of 100 g. 3-chloromethylpyridine-HCl in 600 cc. 60% alc., 7.9 g. KI, and 79 g. KCN refluxed 3 hrs., alc. and H2O removed in vacuo, 300 cc. CHCl3 and 500 cc. satd. soln. of K2CO3 added, and the mixt. heated 30 min. at 40.degree. with vigorous stirring gave 46.5% 3-cyanomethylpyridine (V), b2 100.degree., n20D 1.5260. V (48.4 g.), 238 cc. abs. alc., and 106 cc. dry Et2O cooled to 5.degree., a current of HCl gas bubbled through the soln. for 45 min. while the interior temp. rose to 20-5.degree., the soln. refluxed 5 hrs. with passage of HCl, and kept overnight at room temp. gave 89% Et 3-pyridylacetate, b1 98-100.degree., n20.5D 1.4988. 3-(.beta.-Hydroxyethyl)pyridine (VI) (18.7 g.) in 100 cc. glacial HOAc hydrogenated 3 hrs. in the cold under an initial pressure of 50 kg. in the presence of a 1 g. PtO2 gave 92% 3-(.beta.-hydroxyethyl)piperidine (VII), b4 120-3.degree., n21D 1.4880. A stirred soln. of 12.9 g. VII, 75 cc. CHCl3, and 150 cc. EtMeCO cooled to 5.degree. in the absence of moisture, 10.4 g. indole-3-glyoxalyl chloride in 300 cc. EtMeCO added dropwise over 50 min., and the soln. kept 1 hr. at 0.degree. and then 5 hrs. at room temp. gave 8.3 g. impure VIII. A soln. of 8.3 g. VIII in tetrahydrofuran (THF) was reduced with 6.1 g. LiAlH4 to give 1.3 g. IX, m. 152-3.degree. (MeOH). VI (23.1 g.) and 52 g. 3,4,5-trimethoxybenzoyl chloride in 200 cc. dry pyridine heated 6 hrs. at 80.degree. in a sealed tube gave 83% corresponding ester (X), m. 91.degree. (iso-PrOH). X (12.8 g.) reduced in the cold at atm. pressure in glacial HOAc with PtO2 for 1 hr. gave 84% the piperidino analog (XI) as the HCl salt, m. 233-4.degree. (MeOH). Indole-3-glyoxalyl chloride (XII) (20.6 g.) in THF reduced with 40 g. LiAlH4 and the product hydrolyzed with

aq. KOH <35.degree. gave 78% tryptophol (XIII), m. 56-8.degree.. XIII (6.7 g.) in 250 cc. dry Et2O cooled to -5.degree., 3.8 g. PBr3 in 50 cc. Et2O added over 20 min. at -5.degree., and the mixt. stirred in an ice bath 4 hrs. and 2 days at room temp. gave 100% 3-(.beta.-bromoethyl)indole (XIV). XIV (5.5 g.), 8.85 g. XI, and 3.4 g. K2CO3 in 100 cc. C6H6 refluxed 24 hrs. gave 6% XV.HBr, m. 197.degree. (alc.). Et 3-pyridylacetate (70.7 g.) in 200 cc. glacial HOAc hydrogenated with PtO2 under pressure gave 73% Et 3-piperidinylacetate (XVI), m. 90.degree. (4:1 hexane-C6H6). A soln. of 16.8 g. XII in 460 cc. MeEtCO added with stirring over 20 min. to 26.8 g. XVI in 550 cc. dry EtMeCO, and the mixt. refluxed with stirring 7 hrs. and kept overnight at room temp. gave 30 g. XVII as an oil. XVII (30 g.) in THF reduced with 11.4 g. LiAlH4 gave 14.3 g. IX. A mixt. of 5.1 g. 3,4,5-trimethoxybenzoyl chloride (XVIII) and 5.45 g. IX heated 20 min. at 100.degree. gave 70% XV.HCl, m. 176.degree. (abs. alc.). 6-Methoxyindole-3-glyoxalyl chloride (32.7 g.) in 1650 cc. dry EtMeCO treated with a soln. of 47 g. XVI in 960 cc. EtMeCO, and the mixt. refluxed 4.5 hrs. gave 55 g. 6-methoxy deriv. (XIX) of XVII, an oil, and 3 g. 6-methoxyindole-3-glyoxalic acid, decompd. 272.degree. (HOAc). XlX (55 g.) in THF reduced with 30 g. LiAlH4 gave 14 g. 6-methoxy analog (XX) of IX, m. 139.5.degree. (MeOH); hydrochloride m. 189.degree. (alc.). A mixt. of XX (6.5 g.) and 5.45 g. XVIII heated 20 min. at 90.degree. gave 7.2% 6-methoxy analog (XXI) of XV as HBr salt, m. 140-5.degree.. A soln. of 9.3 g. XIV and 13.2 g. X in 100 cc. Me2CO heated 55 hrs. at 100.degree. in a sealed tube gave 56% XXII, decompd. 232.degree., which forms a solvate in MeOH. XXII (2.8 g.) in 150 cc. 15% HOAc hydrogenated with PtO2 in the cold under atm. pressure gave 67% XV.HBr. 3-(.beta.-Bromoethyl)-6-methoxyindole (1.2 g.) and 1.55 g. X in 30 cc. EtMeCO refluxed 155 hrs. gave 36.5% 6-methoxy analog (XXIII) of XXII, decompd. 203.degree. (iso-PrOH). XXIII (500 mg.) in 30 cc. 15% HOAc hydrogenated with PtO2 in the cold under atm. pressure gave 500 mg. XXI.HBr. XXI.HBr and XV.HBr showed some hypotensive and sedative effects.

IT **94679-94-4**, 3-Piperidineacetic acid, 1-[(6-methoxyindol-3-yl)glyoxyloyl]-, ethyl ester **95277-70-6**, 3-Piperidineacetic acid, 1-(indol-3-ylglyoxyloyl)-, ethyl ester
(prepn. of)

RN 94679-94-4 CAPLUS

CN 3-Piperidineacetic acid, 1-[(6-methoxyindol-3-yl)glyoxyloyl]-, ethyl ester (7CI) (CA INDEX NAME)



RN 95277-70-6 CAPLUS

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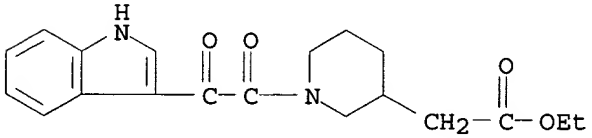

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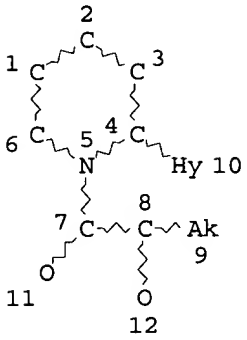

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DEFAULT ECLEVEL IS LIMITED

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RSPEC 1
NUMBER OF NODES IS 12

STEREO ATTRIBUTES: NONE

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SEARCH TIME: 00.00.01

L3 7 SEA SSS FUL L1

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L3 7 ANSWERS REGISTRY COPYRIGHT 2002 ACS
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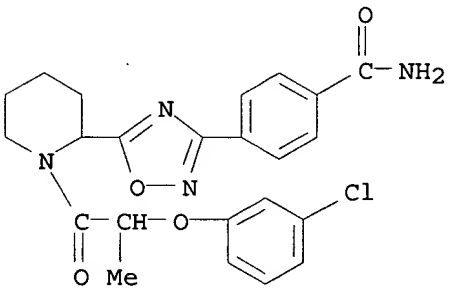
MF C23 H23 Cl N4 O4



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

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FILE COVERS 1907 - 3 Dec 2002  VOL 137 ISS 23
FILE LAST UPDATED: 2 Dec 2002  (20021202/ED)

  This file contains CAS Registry Numbers for easy and accurate
  substance identification.

CAS roles have been modified effective December 16, 2001. Please
check your SDI profiles to see if they need to be revised. For
information on CAS roles, enter HELP ROLES at an arrow prompt or use
the CAS Roles thesaurus (/RL field) in this file.

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L4            4 L3

=> d bib abs hitstr 1-4

L4   ANSWER 1 OF 4  CAPLUS  COPYRIGHT 2002 ACS
AN   2001:50643  CAPLUS
DN   134:115857
TI   Preparation of neurotrophic pyrrolidines and piperidines
IN   Kanojia, Ramesh M.; Jordan, Alfonso D.; Reitz, Allen B.; Macielag, Mark
     J.; Zhao, Boyu
PA   Ortho-McNeil Pharmaceutical, Inc., USA
SO   PCT Int. Appl., 126 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 1
     PATENT NO.         KIND  DATE           APPLICATION NO.  DATE
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             ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU,
             LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD,
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R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL

BR 2000012327 A 20020702 BR 2000-12327 20000614

PRAI US 1999-143006P P 19990709

WO 2000-US16221 W 20000614

OS MARPAT 134:115857

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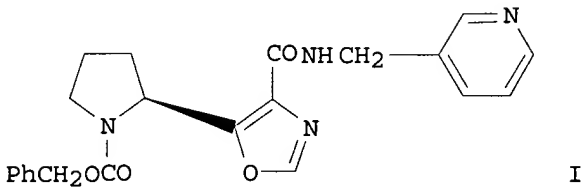


I

AB The title compds. and their neurotrophic activity was detd. E.g., pyrrolidine I was prepd. Nicotinic acetylcholine receptor binding activity was also detd.

IT **320608-05-7P 320608-06-8P 320608-11-5P**

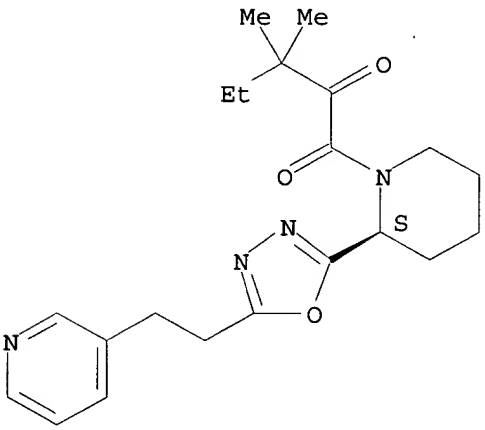
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of neurotrophic pyrrolidines and piperidines)

RN 320608-05-7 CAPLUS

CN Piperidine, 1-(3,3-dimethyl-1,2-dioxopentyl)-2-[5-[2-(3-pyridinyl)ethyl]-1,3,4-oxadiazol-2-yl]-, (2S)- (9CI) (CA INDEX NAME)

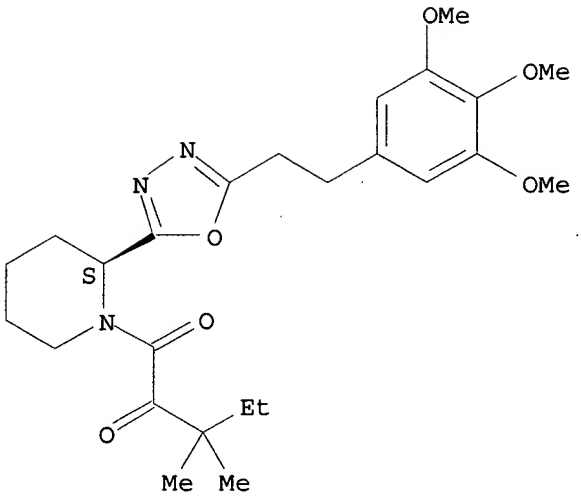
Absolute stereochemistry.



RN 320608-06-8 CAPLUS

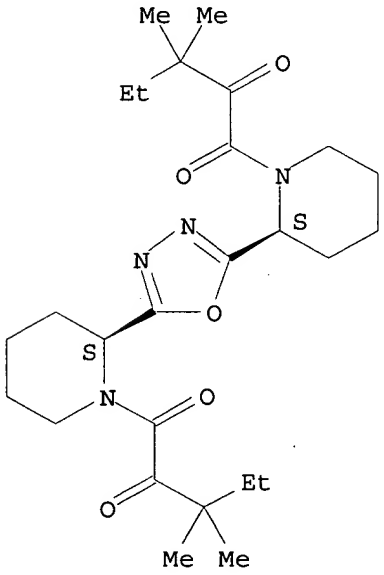
CN Piperidine, 1-(3,3-dimethyl-1,2-dioxopentyl)-2-[5-[2-(3,4,5-trimethoxyphenyl)ethyl]-1,3,4-oxadiazol-2-yl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 320608-11-5 CAPLUS
CN Piperidine, 2,2'-(1,3,4-oxadiazole-2,5-diyl)bis[1-(3,3-dimethyl-1,2-dioxopentyl)-, (2S,2'S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2002 ACS
AN 2000:384175 CAPLUS
DN 133:30959
TI Preparation of prolinylalkanediones and related compounds for treating neurological disease, vision disorders, and alopecia.
IN Hamilton, Gregory S.; Norman, Mark H.; Wu, Yong-qian
PA GPI Nil Holdings, Inc., USA; Amgen, Inc.
SO PCT Int. Appl., 166 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 5

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000032588	A2	20000608	WO 1999-US28663	19991203

	WO 2000032588		A3	20010222											
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		IN,	IS,	JP,	KE,	KG,	KP,	KR,	KZ,	LC,	LK,	LR,	LS,	LT,	LU,	LV,	MA,
		MD,	MG,	MK,	MN,	MW,	MX,	NO,	NZ,	PL,	PT,	RO,	RU,	SD,	SE,	SG,	SI,
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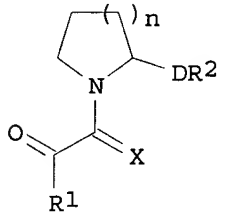


I

AB Title compds. [I; n = 1-3; X = O, S; R1 = (substituted) alkyl, alkenyl, aryl, heteroaryl, carbocyclyl, heterocyclyl; D = bond, (substituted) alkyl, alkenyl, alkynyl; R2 = CO2H, (substituted) CO2H isostere], were prepd. Thus, L-proline Me ester hydrochloride in CH2Cl2 was treated with Et3N and then with MeO2CCOCl to give 88% Me (2S)-1-(1,2-dioxo-2-methoxyethyl)-2-pyrrolidinecarboxylate. The latter in THF at -78.degree. was treated with 1,1-dimethylpropylmagnesium chloride followed by 3 h stirring at -78.degree. to give 75% Me (2S)-1-(1,2-dioxo-3,3-dimethylpentyl)-2-pyrrolidinecarboxylate. This was stirred overnight with aq. LiOH in MeOH to give 87% (2S)-1-(1,2-dioxo-3,3-dimethylpentyl)-2-pyrrolidinecarboxylic acid. In the MPTP model of Parkinson's disease in mice, I at 10 mg/kg orally gave 10.4-46.5% recovery of TH-stained dopaminergic neurons.

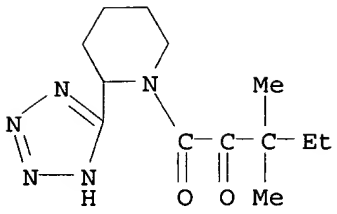
IT **222171-52-0P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of prolinylalkanediones and related compds. for treating neurol. disease, vision disorders, and alopecia)

RN 222171-52-0 CAPLUS

CN Piperidine, 1-(3,3-dimethyl-1,2-dioxopentyl)-2-(1H-tetrazol-5-yl)- (9CI) (CA INDEX NAME)



L4 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2002 ACS
AN 1999:784078 CAPLUS
DN 132:22860
TI Preparation of aza-heterocyclic compounds used to treat neurological disorders and hair loss
IN Hamilton, Gregory S.; Norman, Mark H.; Wu, Yong-Qian; Steiner, Joseph P.
PA Guilford Pharmaceuticals Inc., USA; Amgen, Inc.
SO PCT Int. Appl., 96 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 5

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9962881	A1	19991209	WO 1998-US25573	19981203
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	ZA 9811063	A	20000707	ZA 1998-11063	19981203
	BR 9815920	A	20010220	BR 1998-15920	19981203
	EP 1084107	A1	20010321	EP 1998-961866	19981203
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	NO 2000005903	A	20010202	NO 2000-5903	20001121
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	WO 1998-US25573	W	19981203		

OS MARPAT 132:22860
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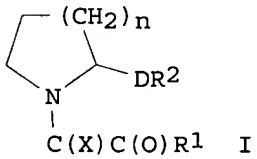


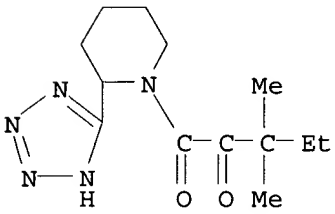
I

AB Prepn. of N-heterocyclic carboxylic acids and carboxylic acid isosteres I [n = 1-3; X = O, S; R1 = C1-C9 straight or branched chain alkyl, C2-C9 straight or branched chain alkenyl, aryl, heteroaryl, carboncycle, heterocycle; D = bond, C1-C10 straight or branched chain alkyl, C2-C10 alkenyl, C2-C10 alkynyl; R2 = carboxylic acid, carboxylic acid isostere]

and their use for treating neurol. disorders and for treating alopecia and promoting hair growth are described. E.g., (2S)-1-(1,2-dioxo-3,3-dimethylpentyl)-2-hydroxymethylpyrrolidine was prepd.

IT **222171-52-0P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of aza-heterocyclic compds. used to treat neurol. disorders and hair loss)

RN 222171-52-0 CAPLUS
CN Piperidine, 1-(3,3-dimethyl-1,2-dioxopentyl)-2-(1H-tetrazol-5-yl)- (9CI) (CA INDEX NAME)



RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2002 ACS
AN 1999:249062 CAPLUS
DN 130:262139
TI Method for treating hearing loss using sensorineurotrophic compounds
IN Magal, Ella
PA Amgen Inc., USA
SO PCT Int. Appl., 649 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 5

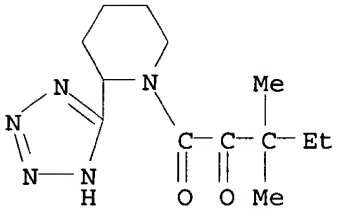
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9914998	A2	19990401	WO 1998-US19980	19980924
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	ZA 9808720	A	19990329	ZA 1998-8720	19980923
	CA 2304647	AA	19990401	CA 1998-2304647	19980924
	AU 9895783	A1	19990412	AU 1998-95783	19980924
	AU 742040	B2	20011213		
	EP 1011650	A1	20000628	EP 1998-949467	19980924
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	JP 2001516767	T2	20011002	JP 2000-512395	19980924
PRAI	US 1997-59905P	P	19970924		
	US 1997-59963P	P	19970925		
	US 1998-159105	A	19980923		
	WO 1998-US19980	W	19980924		

OS MARPAT 130:262139
AB Methods are provided for preventing and/or treating injury or degeneration of inner ear sensory cells, e.g. hair cells and auditory neurons, by

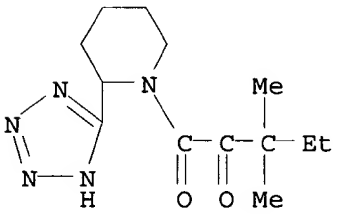
administration of a sensorineurotrophic compd. to a patient in need thereof. Compd. prepn. is included.

IT **222171-52-0 222171-52-0D**, esters
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(sensorineurotrophic compds., and prepn. thereof, for treating hearing loss)

RN 222171-52-0 CAPLUS
CN Piperidine, 1-(3,3-dimethyl-1,2-dioxopentyl)-2-(1H-tetrazol-5-yl)- (9CI) (CA INDEX NAME)



RN 222171-52-0 CAPLUS
CN Piperidine, 1-(3,3-dimethyl-1,2-dioxopentyl)-2-(1H-tetrazol-5-yl)- (9CI) (CA INDEX NAME)

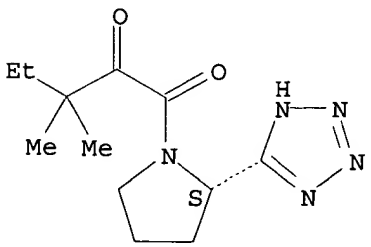


AN 1999:249062 CAPLUS
DN 130:262139
TI Method for treating hearing loss using sensorineurotrophic compounds
IN Magal, Ella
PA Amgen Inc., USA
SO PCT Int. Appl., 649 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 5

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9914998	A2	19990401	WO 1998-US19980	19980924
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	ZA 9808720	A	19990329	ZA 1998-8720	19980923
	CA 2304647	AA	19990401	CA 1998-2304647	19980924
	AU 9895783	A1	19990412	AU 1998-95783	19980924
	AU 742040	B2	20011213		
	EP 1011650	A1	20000628	EP 1998-949467	19980924
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	JP 2001516767	T2	20011002	JP 2000-512395	19980924
PRAI	US 1997-59905P	P	19970924		
	US 1997-59963P	P	19970925		
	US 1998-159105	A	19980923		
	WO 1998-US19980	W	19980924		

OS MARPAT 130:262139
AB Methods are provided for preventing and/or treating injury or degeneration of inner ear sensory cells, e.g. hair cells and auditory neurons, by administration of a sensorineurotrophic compd. to a patient in need thereof. Compd. prepn. is included.
IT **222171-58-6P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(sensorineurotrophic compds., and prepn. thereof, for treating hearing loss)
RN 222171-58-6 CAPLUS
CN Pyrrolidine, 1-(3,3-dimethyl-1,2-dioxopentyl)-2-(1H-tetrazol-5-yl)-, (2S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



AN 2002:353276 CAPLUS
DN 136:369991
TI Preparation of N-acyl heterocyclic compounds as tripeptidyl peptidase inhibitors
IN Breslin, Henry Joseph; De Winter, Hans Louis Jos; Kukla, Michael Joseph
PA Janssen Pharmaceutica N.V., Belg.
SO PCT Int. Appl., 50 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002036116	A2	20020510	WO 2001-EP12388	20011024
	WO 2002036116	A3	20020926		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2002024797	A5	20020515	AU 2002-24797	20011024
PRAI	US 2000-244223P	P	20001030		
	WO 2001-EP12388	W	20011024		

OS MARPAT 136:369991

L4 ANSWER 2 OF 14 CAPLUS COPYRIGHT 2002 ACS
AN 2002:332702 CAPLUS
DN 136:355153
TI Preparation of pyrrolidino and piperidino sulfonamides for treatment of neurological disorders and alopecia
IN Hamilton, Gregory S.; Norman, Mark H.; Wu, Yong-qian
PA USA
SO U.S. Pat. Appl. Publ., 29 pp., Cont.-in-part of U. S. Provisional Ser. No. 87,842.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2002052510	A1	20020502	US 1998-204236	19981203
	ZA 9811060	A	19991203	ZA 1998-11060	19981203
	US 2002052514	A1	20020502	US 2001-791660	20010226
PRAI	US 1998-87842P	P	19980603		
	US 1998-204236	A3	19981203		

OS MARPAT 136:355153

L4 ANSWER 3 OF 14 CAPLUS COPYRIGHT 2002 ACS
AN 2001:916406 CAPLUS
DN 136:31715
TI Carboxylic acids and carboxylic acid isosteres of N-heterocyclic compounds, preparation thereof, and use in the treatment of neurological and other disorders
IN Hamilton, Gregory S.; Norman, Mark H.; Wu, Yong-Qian
PA GPI Nil Holdings, Inc., USA
SO U.S., 62 pp., Cont.-in-part of U.S. Ser. No. 204,237, abandoned.
CODEN: USXXAM
DT Patent

LA English
FAN.CNT 5

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6331537	B1	20011218	US 1999-453571	19991202
	ZA 9811063	A	20000707	ZA 1998-11063	19981203
	WO 2000032588	A2	20000608	WO 1999-US28663	19991203
	WO 2000032588	A3	20010222		
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	BR 9916461	A	20010904	BR 1999-16461	19991203
	EP 1135370	A2	20010926	EP 1999-961930	19991203
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	NO 2001002765	A	20010720	NO 2001-2765	20010605
PRAI	US 1998-87788P	P	19980603		
	US 1998-204237	B2	19981203		
	US 1999-453571	A	19991202		
	WO 1999-US28663	W	19991203		

OS MARPAT 136:31715
RE.CNT 364 THERE ARE 364 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 14 CAPLUS COPYRIGHT 2002 ACS
AN 2001:668212 CAPLUS
DN 135:226999
TI Preparation of 2-azolylpyrrolidine or -piperidine derivatives having neurite outgrowth activity
IN Kato, Susumu; Ueno, Hiroshi; Kondo, Wataru
PA Japan Tobacco, Inc., Japan
SO Jpn. Kokai Tokkyo Koho, 81 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 2001247569	A2	20010911	JP 2000-236882	20000804
PRAI	JP 1999-228938	A	19990812		
	JP 1999-375867	A	19991228		

OS MARPAT 135:226999

L4 ANSWER 5 OF 14 CAPLUS COPYRIGHT 2002 ACS
AN 2001:50643 CAPLUS
DN 134:115857
TI Preparation of neurotrophic pyrrolidines and piperidines
IN Kanojia, Ramesh M.; Jordan, Alfonso D.; Reitz, Allen B.; Macielag, Mark J.; Zhao, Boyu
PA Ortho-McNeil Pharmaceutical, Inc., USA
SO PCT Int. Appl., 126 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

PI WO 2001004116 A2 20010118 WO 2000-US16221 20000614
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
EP 1202990 A2 20020508 EP 2000-939836 20000614
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL
BR 2000012327 A 20020702 BR 2000-12327 20000614
PRAI US 1999-143006P P 19990709
WO 2000-US16221 W 20000614
OS MARPAT 134:115857

L4 ANSWER 6 OF 14 CAPLUS COPYRIGHT 2002 ACS
AN 2000:553576 CAPLUS
DN 133:164058
TI Preparation of 1-gloxyloyl-2-heteroarylpyrrolidines as nerve growth stimulants
IN Brumby, Thomas; McDonald, Fiona; Ottow, Eckhard; Schneider, Herbert
PA Schering Aktiengesellschaft, Germany; Vertex Pharmaceuticals, Inc.
SO PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000046222	A1	20000810	WO 2000-US2660	20000203
DE 19905256	A1	20000810	DE 1999-19905256	19990203
US 6284779	B1	20010904	US 2000-496278	20000201

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RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRAI DE 1999-19905256 A 19990203
US 1999-126007P P 19990324
US 2000-496278 A 20000201
OS MARPAT 133:164058
RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 7 OF 14 CAPLUS COPYRIGHT 2002 ACS
AN 2000:384175 CAPLUS
DN 133:30959
TI Preparation of prolinylalkanediones and related compounds for treating neurological disease, vision disorders, and alopecia.
IN Hamilton, Gregory S.; Norman, Mark H.; Wu, Yong-qian
PA GPI Nil Holdings, Inc., USA; Amgen, Inc.
SO PCT Int. Appl., 166 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 5

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000032588	A2	20000608	WO 1999-US28663	19991203
	WO 2000032588	A3	20010222		
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	RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	US 6331537	B1	20011218	US 1999-453571	19991202
	BR 9916461	A	20010904	BR 1999-16461	19991203
	EP 1135370	A2	20010926	EP 1999-961930	19991203
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	NO 2001002765	A	20010720	NO 2001-2765	20010605
PRAI	US 1998-204237	A	19981203		
	US 1999-453571	A	19991202		
	US 1998-87788P	P	19980603		
	WO 1999-US28663	W	19991203		
OS	MARPAT 133:30959				

L4 ANSWER 8 OF 14 CAPLUS COPYRIGHT 2002 ACS
AN 2000:209809 CAPLUS
DN 132:237375
TI Preparation of bridged heterocyclic derivatives for treatment of neurological and other disorders
IN Li, Jia He; Limburg, David; Hamilton, Gregory S.; Steiner, Joseph P.
PA Guilford Pharmaceuticals Inc., USA
SO PCT Int. Appl., 503 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 5

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000016603	A2	20000330	WO 1998-US25577	19981203
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	CA 2344376	AA	20000330	CA 1998-2344376	19981203
	AU 9919028	A1	20000410	AU 1999-19028	19981203
	EP 1127049	A1	20010829	EP 1998-963776	19981203
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
PRAI	US 1998-101077P	P	19980918		
	US 1998-159105	A	19980923		
	WO 1998-US25577	W	19981203		
OS	MARPAT 132:237375				

L4 ANSWER 9 OF 14 CAPLUS COPYRIGHT 2002 ACS
AN 2000:133473 CAPLUS
DN 132:175844
TI Carboxylic acids and isosteres of N-heterocyclic compounds for vision and memory disorders

IN Ross, Douglas T.; Sauer, Hansjorg; Hamilton, Gregory S.; Steiner, Joseph P.
PA Guilford Pharmaceuticals Inc., USA
SO PCT Int. Appl., 123 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000009102	A2	20000224	WO 1999-US18230	19990812
	WO 2000009102	A3	20000706		
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	RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	CA 2340419	AA	20000224	CA 1999-2340419	19990812
	AU 9954774	A1	20000306	AU 1999-54774	19990812
	EP 1105128	A2	20010613	EP 1999-941050	19990812
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	JP 2002522478	T2	20020723	JP 2000-564605	19990812
PRAI	US 1998-134472	A	19980814		
	WO 1999-US18230	W	19990812		

OS MARPAT 132:175844

L4 ANSWER 10 OF 14 CAPLUS COPYRIGHT 2002 ACS
AN 1999:784085 CAPLUS
DN 132:18814
TI Aza-heterocyclic compounds used to treat neurological disorders and hair loss
IN Hamilton, Gregory S.; Norman, Mark H.; Wu, Yong-Qian; Li, Jia-He; Steiner, Joseph P.
PA Guilford Pharmaceuticals Inc., USA; Amgen, Inc.
SO PCT Int. Appl., 106 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9962888	A1	19991209	WO 1998-US25574	19981203
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	CA 2333964	AA	19991209	CA 1998-2333964	19981203
	AU 9917082	A1	19991220	AU 1999-17082	19981203
	ZA 9811062	A	19991220	ZA 1998-11062	19981203
	BR 9815919	A	20010220	BR 1998-15919	19981203
	EP 1102756	A1	20010530	EP 1998-961867	19981203
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	JP 2002517383	T2	20020618	JP 2000-552100	19981203

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     NO 2000006117     A    20010201       NO 2000-6117     20001201
     US 2002045641     A1   20020418       US 2001-776904   20010206
PRAI US 1998-87843P    P    19980603
     US 1998-204238    A3   19981203
     WO 1998-US25574   W    19981203
OS   MARPAT 132:18814
RE.CNT  6     THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
              ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4   ANSWER 11 OF 14  CAPLUS  COPYRIGHT 2002 ACS
AN   1999:784078  CAPLUS
DN   132:22860
TI   Preparation of aza-heterocyclic compounds used to treat neurological
     disorders and hair loss
IN   Hamilton, Gregory S.; Norman, Mark H.; Wu, Yong-Qian; Steiner, Joseph P.
PA   Guilford Pharmaceuticals Inc., USA; Amgen, Inc.
SO   PCT Int. Appl., 96 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 5
     PATENT NO.        KIND  DATE           APPLICATION NO.  DATE
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PI   WO 9962881         A1   19991209       WO 1998-US25573  19981203
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             KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW,
             MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR,
             TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
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             CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
     CA 2333963        AA   19991209       CA 1998-2333963  19981203
     AU 9917081        A1   19991220       AU 1999-17081    19981203
     ZA 9811063        A    20000707       ZA 1998-11063    19981203
     BR 9815920        A    20010220       BR 1998-15920    19981203
     EP 1084107        A1   20010321       EP 1998-961866   19981203
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     JP 2002516905     T2   20020611       JP 2000-552093   19981203
     NO 2000005903     A    20010202       NO 2000-5903     20001121
PRAI US 1998-87788P    P    19980603
     US 1998-101077P   P    19980918
     WO 1998-US25573   W    19981203
OS   MARPAT 132:22860
RE.CNT  7     THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
              ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4   ANSWER 12 OF 14  CAPLUS  COPYRIGHT 2002 ACS
AN   1999:784077  CAPLUS
DN   132:18813
TI   N-linked sulfonamides of N-heterocyclic carboxylic acids or carboxylic
     acid isosteres for treatment of neurological disorders and alopecia
IN   Hamilton, Gregory S.; Norman, Mark H.; Wu, Yong-Qian
PA   Guilford Pharmaceuticals Inc., USA; Amgen, Inc.
SO   PCT Int. Appl., 96 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 2
     PATENT NO.        KIND  DATE           APPLICATION NO.  DATE
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PI   WO 9962880         A1   19991209       WO 1998-US25572  19981203
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            KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW,
            MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR,
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    ZA 9811060        A    19991203       ZA 1998-11060    19981203
    CA 2334002        AA   19991209       CA 1998-2334002  19981203
    AU 9917080        A1   19991220       AU 1999-17080    19981203
    EP 1084106        A1   20010321       EP 1998-961865   19981203
        R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
            IE, SI, LT, LV, FI, RO
    JP 2002516904     T2   20020611       JP 2000-552092   19981203
    BR 9815882        A    20020917       BR 1998-15882    19981203
    NO 2000006078     A    20010205       NO 2000-6078     20001130
PRAI US 1998-87842P   P    19980603
    WO 1998-US25572   W    19981203
OS  MARPAT 132:18813
RE.CNT  7     THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
              ALL CITATIONS AVAILABLE IN THE RE FORMAT
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AN 1999:249062 CAPLUS
DN 130:262139
TI Method for treating hearing loss using sensorineurotrophic compounds
IN Magal, Ella
PA Amgen Inc., USA
SO PCT Int. Appl., 649 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 5

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9914998	A2	19990401	WO 1998-US19980	19980924
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	ZA 9808720	A	19990329	ZA 1998-8720	19980923
	CA 2304647	AA	19990401	CA 1998-2304647	19980924
	AU 9895783	A1	19990412	AU 1998-95783	19980924
	AU 742040	B2	20011213		
	EP 1011650	A1	20000628	EP 1998-949467	19980924
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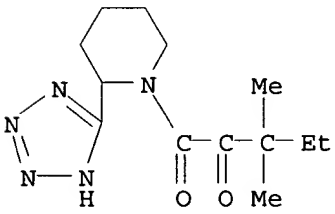
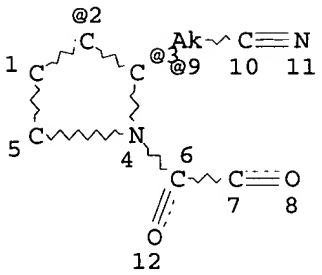
	JP 2001516767	T2	20011002	JP 2000-512395	19980924
PRAI	US 1997-59905P	P	19970924		
	US 1997-59963P	P	19970925		
	US 1998-159105	A	19980923		
	WO 1998-US19980	W	19980924		

OS MARPAT 130:262139
AB Methods are provided for preventing and/or treating injury or degeneration of inner ear sensory cells, e.g. hair cells and auditory neurons, by administration of a sensorineurotrophic compd. to a patient in need thereof. Compd. prepn. is included.
IT **222171-52-0 222171-52-0D**, esters
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(sensorineurotrophic compds., and prepn. thereof, for treating hearing loss)
RN 222171-52-0 CAPLUS
CN Piperidine, 1-(3,3-dimethyl-1,2-dioxopentyl)-2-(1H-tetrazol-5-yl)- (9CI) (CA INDEX NAME)



RN 222171-52-0 CAPLUS
CN Piperidine, 1-(3,3-dimethyl-1,2-dioxopentyl)-2-(1H-tetrazol-5-yl)- (9CI) (CA INDEX NAME)



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BATCH **COMPLETE**
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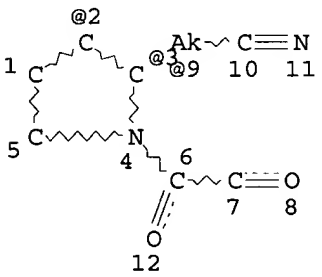

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STEREO ATTRIBUTES: NONE

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100.0% PROCESSED 1328 ITERATIONS 4 ANSWERS

SEARCH TIME: 00.00.01

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FULL ESTIMATED COST	141.80	487.28

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
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FILE COVERS 1907 - 3 Dec 2002 VOL 137 ISS 23
FILE LAST UPDATED: 2 Dec 2002 (20021202/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

CAS roles have been modified effective December 16, 2001. Please check your SDI profiles to see if they need to be revised. For information on CAS roles, enter HELP ROLES at an arrow prompt or use the CAS Roles thesaurus (/RL field) in this file.

=> s l14
L15 3 L14

=> d bib abs hitstr 3

L15 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2002 ACS
AN 1999:784078 CAPLUS
DN 132:22860
TI Preparation of aza-heterocyclic compounds used to treat neurological disorders and hair loss
IN Hamilton, Gregory S.; Norman, Mark H.; Wu, Yong-Qian; Steiner, Joseph P.
PA Guilford Pharmaceuticals Inc., USA; Amgen, Inc.
SO PCT Int. Appl., 96 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 5

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9962881	A1	19991209	WO 1998-US25573	19981203

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW,

MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR,
TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES,
FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI,
CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

	CA 2333963	AA	19991209	CA 1998-2333963	19981203
	AU 9917081	A1	19991220	AU 1999-17081	19981203
	ZA 9811063	A	20000707	ZA 1998-11063	19981203
	BR 9815920	A	20010220	BR 1998-15920	19981203
	EP 1084107	A1	20010321	EP 1998-961866	19981203
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	JP 2002516905	T2	20020611	JP 2000-552093	19981203
	NO 2000005903	A	20010202	NO 2000-5903	20001121
PRAI	US 1998-87788P	P	19980603		
	US 1998-101077P	P	19980918		
	WO 1998-US25573	W	19981203		

OS MARPAT 132:22860
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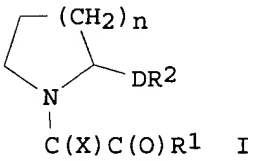

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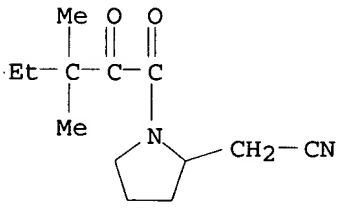
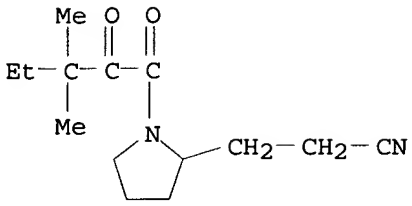
AB Prepn. of N-heterocyclic carboxylic acids and carboxylic acid isosteres I [n = 1-3; X = O, S; R1 = C1-C9 straight or branched chain alkyl, C2-C9 straight or branched chain alkenyl, aryl, heteroaryl, carboncycle, heterocycle; D = bond, C1-C10 straight or branched chain alkyl, C2-C10 alkenyl, C2-C10 alkynyl; R2 = carboxylic acid, carboxylic acid isostere] and their use for treating neurol. disorders and for treating alopecia and promoting hair growth are described. E.g., (2S)-1-(1,2-dioxo-3,3-dimethylpentyl)-2-hydroxymethylpyrrolidine was prepd.

IT **251949-41-4P 251950-09-1P 251950-10-4P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of aza-heterocyclic compds. used to treat neurol. disorders and hair loss)

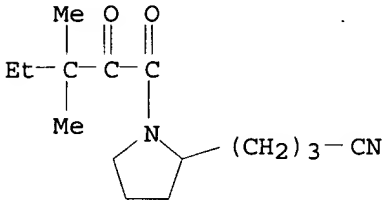
RN 251949-41-4 CAPLUS
CN 2-Pyrrolidineacetonitrile, 1-(3,3-dimethyl-1,2-dioxopentyl)- (9CI) (CA INDEX NAME)



RN 251950-09-1 CAPLUS
CN 2-Pyrrolidinepropanenitrile, 1-(3,3-dimethyl-1,2-dioxopentyl)- (9CI) (CA INDEX NAME)



RN 251950-10-4 CAPLUS
CN 2-Pyrrolidinebutanenitrile, 1-(3,3-dimethyl-1,2-dioxopentyl)- (9CI) (CA INDEX NAME)



RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d bib abs 1-2

L15 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2002 ACS
AN 2001:916406 CAPLUS
DN 136:31715
TI Carboxylic acids and carboxylic acid isosteres of N-heterocyclic compounds, preparation thereof, and use in the treatment of neurological and other disorders
IN Hamilton, Gregory S.; Norman, Mark H.; Wu, Yong-Qian
PA GPI Nil Holdings, Inc., USA
SO U.S., 62 pp., Cont.-in-part of U.S. Ser. No. 204,237, abandoned.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 5

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6331537	B1	20011218	US 1999-453571	19991202
	ZA 9811063	A	20000707	ZA 1998-11063	19981203
	WO 2000032588	A2	20000608	WO 1999-US28663	19991203
	WO 2000032588	A3	20010222		
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	BR 9916461	A	20010904	BR 1999-16461	19991203
	EP 1135370	A2	20010926	EP 1999-961930	19991203
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	NO 2001002765	A	20010720	NO 2001-2765	20010605
PRAI	US 1998-87788P	P	19980603		

US 1998-204237 B2 19981203
US 1999-453571 A 19991202
WO 1999-US28663 W 19991203
OS MARPAT 136:31715
AB N-heterocyclic carboxylic acids and carboxylic acid isosteres are provided, as are their prepn. and their use for treating neurol. disorders including phys. damaged nerves and neurodegenerative diseases, for treating alopecia and promoting hair growth, for treating vision disorders and/or improving vision, and for treating memory impairment and/or enhancing memory performance by administering such compds.
RE.CNT 364 THERE ARE 364 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2002 ACS
AN 2000:384175 CAPLUS
DN 133:30959
TI Preparation of prolinylalkanediones and related compounds for treating neurological disease, vision disorders, and alopecia.
IN Hamilton, Gregory S.; Norman, Mark H.; Wu, Yong-qian
PA GPI Nil Holdings, Inc., USA; Amgen, Inc.
SO PCT Int. Appl., 166 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 5

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2000032588	A2	20000608	WO 1999-US28663	19991203
WO 2000032588	A3	20010222		
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BR 9916461	A	20010904	BR 1999-16461	19991203
EP 1135370	A2	20010926	EP 1999-961930	19991203
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US 1998-87788P P 19980603
WO 1999-US28663 W 19991203
OS MARPAT 133:30959
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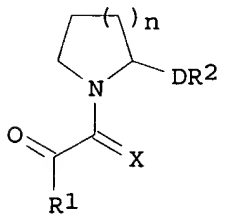

I

AB Title compds. [I; n = 1-3; X = O, S; R1 = (substituted) alkyl, alkenyl, aryl, heteroaryl, carbocyclyl, heterocyclyl; D = bond, (substituted) alkyl, alkenyl, alkynyl; R2 = CO2H, (substituted) CO2H isostere], were prepd. Thus, L-proline Me ester hydrochloride in CH2Cl2 was treated with Et3N and then with MeO2CCOCl to give 88% Me (2S)-1-(1,2-dioxo-2-methoxyethyl)-2-pyrrolidinecarboxylate. The latter in THF at -78.degree. was treated with 1,1-dimethylpropylmagnesium chloride followed by 3 h stirring at -78.degree. to give 75% Me (2S)-1-(1,2-dioxo-3,3-dimethylpentyl)-2-pyrrolidinecarboxylate. This was stirred overnight with aq. LiOH in MeOH to give 87% (2S)-1-(1,2-dioxo-3,3-dimethylpentyl)-2-pyrrolidinecarboxylic acid. In the MPTP model of Parkinson's disease in mice, I at 10 mg/kg orally gave 10.4-46.5% recovery of TH-stained dopaminergic neurons.

AN 2000:335380 CAPLUS
DN 132:334359
TI Preparation of pyrrolidinylmethyl aralkylcarbamates as FKBP12 inhibitors
IN Dubowchik, Gene M.; Ditta, Jonathan L.; Provencal, David P.; Denhart, Derek J.
PA Bristol-Myers Squibb Company, USA
SO PCT Int. Appl., 74 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000027811	A1	20000518	WO 1999-US26798	19991109
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	US 6228872	B1	20010508	US 1999-435529	19991108
	EP 1129070	A1	20010905	EP 1999-960305	19991109
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	AU 751541	B2	20020822	AU 2000-17205	19991109
	JP 2002529449	T2	20020910	JP 2000-580991	19991109
PRAI	US 1998-108060P	P	19981112		
	WO 1999-US26798	W	19991109		

OS MARPAT 132:334359
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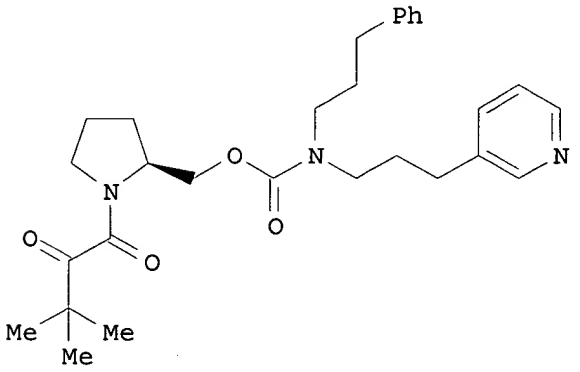


II

AB R1Z1CONR2CHR3CR4R5ZCONR6R7 [I; R1 = alk(en)yl(oxy), (hetero)aryl, etc.; R2,R4,R5 = H, alkyl, CH2Ph; R3 = alkyl, CH2Ph, cyclohexylmethyl; R2R3 = atoms to complete a ring; R6,R7 = H, (ar)alkyl, (hetero)aryl, etc.; Z = O, CH2, (alkyl)imino; Z1 = CO ro CF2] were prepd. Thus, R(CH2)3NH(CH2)3Ph (R = 3-pyridyl) was amidated by N-trimethylpyruvyl-L-pyrrolidinylmethyl p-nitrophenylcarbonate (prepn each given) to give title compd. II. Data for biol. activity of I were given.

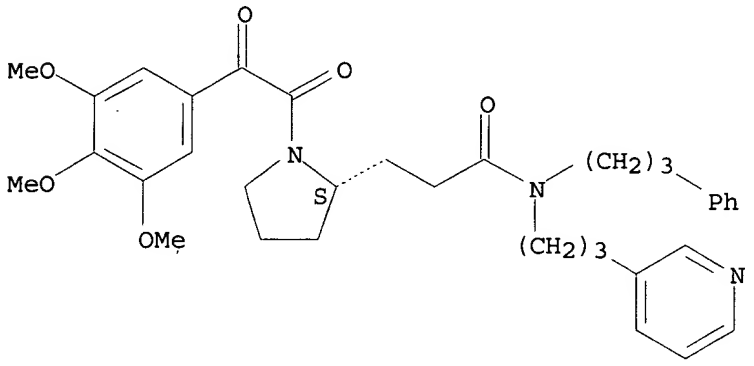
IT **267887-84-3P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of pyrrolidinylmethyl aralkylcarbamates as FKBP12 inhibitors)

RN 267887-84-3 CAPLUS

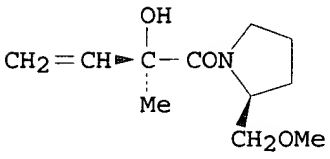
CN 2-Pyrrolidinepropanamide, 1-[oxo(3,4,5-trimethoxyphenyl)acetyl]-N-(3-phenylpropyl)-N-[3-(3-pyridinyl)propyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

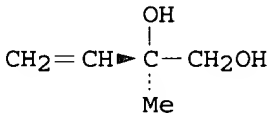


RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

AN 1987:119239 CAPLUS
DN 106:119239
TI The formation and alkylation of .alpha.-keto amide dianions
AU Koft, Emil R.; Williams, Michael D.
CS Dep. Chem., Rensselaer Polytech. Inst., Troy, NY, 12180-3590, USA
SO Tetrahedron Letters (1986), 27(20), 2227-30
CODEN: TELEAY; ISSN: 0040-4039
DT Journal
LA English
OS CASREACT 106:119239
GI



III



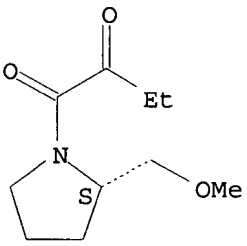
IV

AB Three title compds. RCH2COCONR12 [I; R = Me, Et; R12N = Et2N; R = Me, R12N = 2-(methoxymethyl)pyrrolidino (II)] were doubly deprotonated with LiN(CHMe2)2. Treatment with R3X(R3 = Me, Pr, allyl, CH2:CMeCH2CH2; X = Br, iodo) gave 6 HOCR3R4CONR1R2 (same R1-R3; R4 = CH:CH2, CH:CHMe) in 29-84% yield. Chiral II gave III as a mixt. of diastereomers, which gave optically active diol IV on hydride redn.

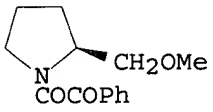
IT **107210-15-1**
RL: RCT (Reactant); RACT (Reactant or reagent)
(condensation of, with alkyl halides, .alpha.-amido tertiary alcs. by)

RN 107210-15-1 CAPLUS
CN Pyrrolidine, 1-(1,2-dioxobutyl)-2-(methoxymethyl)-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



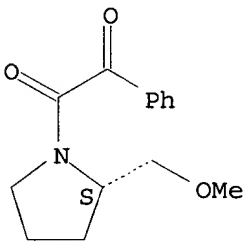
AN 1988:150009 CAPLUS
DN 108:150009
TI Asymmetric reactions with amide derivatives of (S)-prolinyl methyl ether. I. Synthesis of (R)-atrolactic acid by an asymmetric Grignard reaction
AU Suzuki, Kojiro; Sakakiyama, Etsuko; Fujiyama, Ryoji
CS Fac. Sci., Kochi Univ., Kochi, 780, Japan
SO Kochi Daigaku Rigakubu Kiyo, Kagaku (1987), 8, 51-7
CODEN: KDRKDD; ISSN: 0389-0279
DT Journal
LA Japanese
GI



I

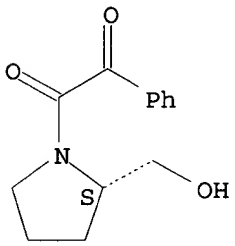
AB Grignard reaction of (S)-N-acylprolinyl Me ether I with MeMgI gives, after hydrolysis with Na2O2, (R)-HOCMePhCO2H in 81% enantiomeric excess. The stereochem. of the addn. comes from chelation of Mg with both the carbonyl and methoxy oxygens.
IT **113742-94-2**
RL: RCT (Reactant); RACT (Reactant or reagent)
(stereoselective Grignard reaction of, with methylmagnesium iodide)
RN 113742-94-2 CAPLUS
CN Pyrrolidine, 2-(methoxymethyl)-1-(oxophenylacetyl)-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



AN 1995:760472 CAPLUS
DN 123:339285
TI Stereodivergent approach to .alpha.-hydroxy acids involving substrate directed reduction of .alpha.-keto amides
AU Pansare, Sunil V.; Ravi, R. Gnana
CS Div. Org. Chem., Natl. Chem. Lab., Pune, 411 008, India
SO Tetrahedron Letters (1995), 36(33), 5959-62
CODEN: TELEAY; ISSN: 0040-4039
PB Elsevier
DT Journal
LA English
OS CASREACT 123:339285
AB Substrate directed redn. of 'S'-2-hydroxymethylpyrrolidine derived .alpha.-keto amides with tetramethylammonium triacetoxyborohydride proceeds with good stereoselectivity at room temp. A reversal of stereoselectivity is obsd. in redns. with conventional borohydride reducing agents in protic solvents.
IT **170945-11-6**
RL: PEP (Physical, engineering or chemical process); RCT (Reactant); PROC (Process); RACT (Reactant or reagent)
(synthesis of .alpha.-hydroxy acids by substrate directed redn. of .alpha.-keto amides)
RN 170945-11-6 CAPLUS
CN 2-Pyrrolidinemethanol, 1-(oxophenylacetyl)-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

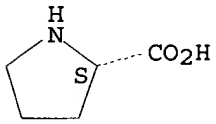


AN 2001:687445 CAPLUS
DN 135:236450
TI Prolyl ester compound inhibitors of rotamase activity, their preparation, and their use
IN Hamilton, Gregory S.; Steiner, Joseph P.
PA GPI NIL Holdings, Inc., USA
SO U.S., 20 pp., Cont.-in-part of U. S. 693,003.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 8

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6291510	B1	20010918	US 1998-73962	19980507
	US 5614547	A	19970325	US 1995-479436	19950607
PRAI	US 1995-479436	A1	19950607		
	US 1996-693003	A2	19960806		

OS MARPAT 135:236450
AB The invention provides neurotrophic compds. having an affinity for FKBP-type immunophilins, their prepn., and their use as inhibitors of the enzyme activity assocd. with immunophilin proteins, and particularly inhibitors of peptidyl-prolyl isomerase or rotamase enzyme activity. The compds. of the invention may be used in the treatment of neurol. disorders, the prevention of neurodegeneration, and the promotion of neuronal regeneration and growth.
IT **147-85-3D**, Proline, derivs.
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prolyl ester compd. inhibitors of **rotamase** activity, prepn., and use)
RN 147-85-3 CAPLUS
CN L-Proline (9CI) (CA INDEX NAME)

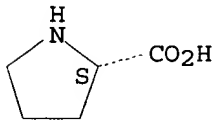
Absolute stereochemistry. Rotation (-).



RE.CNT 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

AN 1999:39083 CAPLUS
DN 130:206459
TI Specific interaction between bovine cyclophilin A and synthetic analogs of cyclolinopeptide A
AU Gallo, Pasquale; Rossi, Filomena; Saviano, Michele; Pedone, Carlo; Colonna, Giovanni; Ragone, Raffaele
CS Centro di Studio di Biocristallografia del C.N.R., Dipartimento di Chimica, Universita degli Studi di Napoli "Federico II,", Naples, 80134, Italy
SO Journal of Biochemistry (Tokyo) (1998), 124(5), 880-885
CODEN: JOBIAO; ISSN: 0021-924X
PB Japanese Biochemical Society
DT Journal
LA English
AB Like cyclosporin A, cyclolinopeptide A binds specifically bovine cyclophilin A, inhibiting its peptidyl-prolyl cis-trans isomerase activity. We describe here the protein interaction with several synthetic analogs of cyclolinopeptide A, which are either homodetic or disulfide bridged heterodetic cyclopeptides characterized by different ring dimensions, in terms of dissocn. and inhibition consts. evaluated by fluorescence and inhibition of the enzyme activity, resp. Dissocn. consts. from fluorescence expts. are practically identical and about 20-fold lower than for cyclosporin A. On the other hand, inhibition consts. differ from compd. to compd. and are higher than for cyclosporin A. This result is therefore difficult to rationalize, but we would suggest decoupling between binding and inhibitory ability of cyclopeptides. The Pro1 residue of cyclolinopeptide A seems to play a fundamental role in detg. the inhibition of the rotamase activity of cyclophilin A, as the homodetic analog lacking this residue does not show any inhibitory ability. Similarly, heterodetic analogs with a ring size smaller than 7 residues do not display inhibition. We presume that the sequence -Pro-Pro-Phe-Phe- and a ring size of 8 residues for homodetic cyclic peptides could be used as starting points in the targeted synthesis of cyclopeptides able to bind both cyclosporin A and calcineurin. The only peptide showing similar values of the dissocn. and inhibition const. is cyclolinopeptide A. This compd. can be considered a novel model for the mol. design of immunosuppressant drugs.
IT **147-85-3**, L-Proline, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(fundamental role of Pro1 in the inhibition of cyclophilin A **rotamase** activity by cyclolinopeptide A; specific interaction between bovine cyclophilin A and synthetic analogs of cyclolinopeptide A)
RN 147-85-3 CAPLUS
CN L-Proline (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RE.CNT 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

AN 1998:630180 CAPLUS
DN 130:25277
TI Intramolecular Catalysis of Amide Isomerization: Kinetic Consequences of the 5-NH- -Na Hydrogen Bond in Prolyl Peptides
AU Cox, Christopher; Lectka, Thomas
CS Department of Chemistry, Johns Hopkins University, Baltimore, MD, 21218, USA
SO Journal of the American Chemical Society (1998), 120(41), 10660-10668
CODEN: JACSAT; ISSN: 0002-7863
PB American Chemical Society
DT Journal
LA English
RE.CNT 66 THERE ARE 66 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
AB The presence of an intramol. hydrogen bond has been proposed to play a key role in the catalysis of amide isomerization by peptidylprolyl isomerases (PPIases), which are highly conserved and ubiquitous **rotamase** enzymes that catalyze the cis-trans isomerization of **proline** residues in peptides and proteins. The authors present kinetic and spectroscopic evidence that indicates the existence of an intramol. hydrogen bond between the prolyl amide nitrogen and the adjacent amidic NH within a five-membered ring (the 5-NH-to-Na hydrogen bond) that is capable of catalyzing **proline** isomerization by up to 260-fold in model prolyl peptides. These results provide the first systematic study of intramol. general-**acid**-catalyzed amide isomerization.

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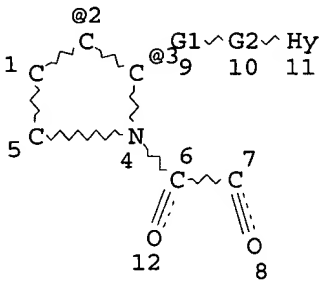
L1 STR



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DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC 3
NUMBER OF NODES IS 12

STEREO ATTRIBUTES: NONE

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100.0% PROCESSED 52167 ITERATIONS 65 ANSWERS
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FULL ESTIMATED COST	141.04	141.25

FILE 'CAPLUS' ENTERED AT 12:05:50 ON 04 DEC 2002

FILE COVERS 1907 - 4 Dec 2002 VOL 137 ISS 23
FILE LAST UPDATED: 3 Dec 2002 (20021203/ED)

This file contains CAS Registry Numbers for easy and accurate

substance identification.

CAS roles have been modified effective December 16, 2001. Please check your SDI profiles to see if they need to be revised. For information on CAS roles, enter HELP ROLES at an arrow prompt or use the CAS Roles thesaurus (/RL field) in this file.

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=> s l3
L4          12 L3

=> d hitstr 12

L4   ANSWER 12 OF 12  CAPLUS  COPYRIGHT 2002 ACS
IT   222171-58-6P
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);
     BIOL (Biological study); PREP (Preparation); USES (Uses)
        (sensorineurotrophic compds., and prepn. thereof, for treating hearing
        loss)
RN   222171-58-6  CAPLUS
CN   Pyrrolidine, 1-(3,3-dimethyl-1,2-dioxopentyl)-2-(1H-tetrazol-5-yl)-, (2S)-
     (9CI)  (CA INDEX NAME)

Absolute stereochemistry.
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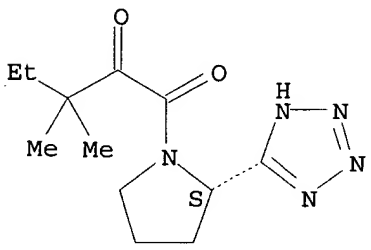


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=> d bib 12

L4   ANSWER 12 OF 12  CAPLUS  COPYRIGHT 2002 ACS
AN   1999:249062  CAPLUS
DN   130:262139
TI   Method for treating hearing loss using sensorineurotrophic compounds
IN   Magal, Ella
PA   Amgen Inc., USA
SO   PCT Int. Appl., 649 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 5
     PATENT NO.         KIND  DATE          APPLICATION NO.  DATE
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PI   WO 9914998          A2   19990401      WO 1998-US19980  19980924
         W:  AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,
             DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG,
             KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX,
             NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT,
             UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
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             CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
     ZA 9808720          A    19990329      ZA 1998-8720     19980923
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	CA 2304647	AA	19990401	CA 1998-2304647	19980924
	AU 9895783	A1	19990412	AU 1998-95783	19980924
	AU 742040	B2	20011213		
	EP 1011650	A1	20000628	EP 1998-949467	19980924
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	JP 2001516767	T2	20011002	JP 2000-512395	19980924
PRAI	US 1997-59905P	P	19970924		
	US 1997-59963P	P	19970925		
	US 1998-159105	A	19980923		
	WO 1998-US19980	W	19980924		
OS	MARPAT 130:262139				

=> d bib 1-11

L4 ANSWER 1 OF 12 CAPLUS COPYRIGHT 2002 ACS
AN 2002:332702 CAPLUS
DN 136:355153
TI Preparation of pyrrolidino and piperidino sulfonamides for treatment of neurological disorders and alopecia
IN Hamilton, Gregory S.; Norman, Mark H.; Wu, Yong-qian
PA USA
SO U.S. Pat. Appl. Publ., 29 pp., Cont.-in-part of U. S. Provisional Ser. No. 87,842.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2002052510	A1	20020502	US 1998-204236	19981203
	ZA 9811060	A	19991203	ZA 1998-11060	19981203
	US 2002052514	A1	20020502	US 2001-791660	20010226
PRAI	US 1998-87842P	P	19980603		
	US 1998-204236	A3	19981203		

OS MARPAT 136:355153

L4 ANSWER 2 OF 12 CAPLUS COPYRIGHT 2002 ACS
AN 2001:916406 CAPLUS
DN 136:31715
TI Carboxylic acids and carboxylic acid isosteres of N-heterocyclic compounds, preparation thereof, and use in the treatment of neurological and other disorders
IN Hamilton, Gregory S.; Norman, Mark H.; Wu, Yong-Qian
PA GPI Nil Holdings, Inc., USA
SO U.S., 62 pp., Cont.-in-part of U.S. Ser. No. 204,237, abandoned.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 5

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6331537	B1	20011218	US 1999-453571	19991202
	ZA 9811063	A	20000707	ZA 1998-11063	19981203
	WO 2000032588	A2	20000608	WO 1999-US28663	19991203
	WO 2000032588	A3	20010222		
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	BR 9916461	A	20010904	BR 1999-16461	19991203
	EP 1135370	A2	20010926	EP 1999-961930	19991203
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	NO 2001002765	A	20010720	NO 2001-2765	20010605
PRAI	US 1998-87788P	P	19980603		
	US 1998-204237	B2	19981203		
	US 1999-453571	A	19991202		
	WO 1999-US28663	W	19991203		

OS MARPAT 136:31715

RE.CNT 364 THERE ARE 364 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 12 CAPLUS COPYRIGHT 2002 ACS
AN 2001:668212 CAPLUS
DN 135:226999
TI Preparation of 2-azolylpyrrolidine or -piperidine derivatives having neurite outgrowth activity
IN Kato, Susumu; Ueno, Hiroshi; Kondo, Wataru
PA Japan Tobacco, Inc., Japan
SO Jpn. Kokai Tokkyo Koho, 81 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 2001247569	A2	20010911	JP 2000-236882	20000804
PRAI	JP 1999-228938	A	19990812		
	JP 1999-375867	A	19991228		

OS MARPAT 135:226999

L4 ANSWER 4 OF 12 CAPLUS COPYRIGHT 2002 ACS
AN 2001:50643 CAPLUS
DN 134:115857
TI Preparation of neurotrophic pyrrolidines and piperidines
IN Kanojia, Ramesh M.; Jordan, Alfonso D.; Reitz, Allen B.; Macielag, Mark J.; Zhao, Boyu
PA Ortho-McNeil Pharmaceutical, Inc., USA
SO PCT Int. Appl., 126 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001004116	A2	20010118	WO 2000-US16221	20000614
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	EP 1202990	A2	20020508	EP 2000-939836	20000614
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
	BR 2000012327	A	20020702	BR 2000-12327	20000614
PRAI	US 1999-143006P	P	19990709		
	WO 2000-US16221	W	20000614		

OS MARPAT 134:115857

L4 ANSWER 5 OF 12 CAPLUS COPYRIGHT 2002 ACS
AN 2000:553576 CAPLUS
DN 133:164058
TI Preparation of 1-gloxyloyl-2-heteroarylpyrrolidines as nerve growth stimulants
IN Brumby, Thomas; McDonald, Fiona; Ottow, Eckhard; Schneider, Herbert
PA Schering Aktiengesellschaft, Germany; Vertex Pharmaceuticals, Inc.
SO PCT Int. Appl., 37 pp.
CODEN: PIXXD2

DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000046222	A1	20000810	WO 2000-US2660	20000203
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	DE 19905256	A1	20000810	DE 1999-19905256	19990203
	US 6284779	B1	20010904	US 2000-496278	20000201
PRAI	DE 1999-19905256	A	19990203		
	US 1999-126007P	P	19990324		
	US 2000-496278	A	20000201		

OS MARPAT 133:164058
RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 6 OF 12 CAPLUS COPYRIGHT 2002 ACS
AN 2000:384175 CAPLUS
DN 133:30959
TI Preparation of prolinylalkanediones and related compounds for treating neurological disease, vision disorders, and alopecia.
IN Hamilton, Gregory S.; Norman, Mark H.; Wu, Yong-qian
PA GPI Nil Holdings, Inc., USA; Amgen, Inc.
SO PCT Int. Appl., 166 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 5

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000032588	A2	20000608	WO 1999-US28663	19991203
	WO 2000032588	A3	20010222		
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	US 6331537	B1	20011218	US 1999-453571	19991202
	BR 9916461	A	20010904	BR 1999-16461	19991203
	EP 1135370	A2	20010926	EP 1999-961930	19991203
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	NO 2001002765	A	20010720	NO 2001-2765	20010605
PRAI	US 1998-204237	A	19981203		
	US 1999-453571	A	19991202		
	US 1998-87788P	P	19980603		
	WO 1999-US28663	W	19991203		

OS MARPAT 133:30959

L4 ANSWER 7 OF 12 CAPLUS COPYRIGHT 2002 ACS
AN 2000:209809 CAPLUS

DN 132:237375
TI Preparation of bridged heterocyclic derivatives for treatment of neurological and other disorders
IN Li, Jia He; Limburg, David; Hamilton, Gregory S.; Steiner, Joseph P.
PA Guilford Pharmaceuticals Inc., USA
SO PCT Int. Appl., 503 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 5

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000016603	A2	20000330	WO 1998-US25577	19981203
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	CA 2344376	AA	20000330	CA 1998-2344376	19981203
	AU 9919028	A1	20000410	AU 1999-19028	19981203
	EP 1127049	A1	20010829	EP 1998-963776	19981203
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
PRAI	US 1998-101077P	P	19980918		
	US 1998-159105	A	19980923		
	WO 1998-US25577	W	19981203		

OS MARPAT 132:237375

L4 ANSWER 8 OF 12 CAPLUS COPYRIGHT 2002 ACS
AN 2000:133473 CAPLUS
DN 132:175844
TI Carboxylic acids and isosteres of N-heterocyclic compounds for vision and memory disorders
IN Ross, Douglas T.; Sauer, Hansjorg; Hamilton, Gregory S.; Steiner, Joseph P.
PA Guilford Pharmaceuticals Inc., USA
SO PCT Int. Appl., 123 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000009102	A2	20000224	WO 1999-US18230	19990812
	WO 2000009102	A3	20000706		
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	CA 2340419	AA	20000224	CA 1999-2340419	19990812
	AU 9954774	A1	20000306	AU 1999-54774	19990812
	EP 1105128	A2	20010613	EP 1999-941050	19990812
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	JP 2002522478	T2	20020723	JP 2000-564605	19990812

PRAI US 1998-134472 A 19980814
WO 1999-US18230 W 19990812
OS MARPAT 132:175844

L4 ANSWER 9 OF 12 CAPLUS COPYRIGHT 2002 ACS
AN 1999:784085 CAPLUS
DN 132:18814
TI Aza-heterocyclic compounds used to treat neurological disorders and hair loss
IN Hamilton, Gregory S.; Norman, Mark H.; Wu, Yong-Qian; Li, Jia-He; Steiner, Joseph P.
PA Guilford Pharmaceuticals Inc., USA; Amgen, Inc.
SO PCT Int. Appl., 106 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9962888	A1	19991209	WO 1998-US25574	19981203
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2333964	AA	19991209	CA 1998-2333964	19981203
AU 9917082	A1	19991220	AU 1999-17082	19981203
ZA 9811062	A	19991220	ZA 1998-11062	19981203
BR 9815919	A	20010220	BR 1998-15919	19981203
EP 1102756	A1	20010530	EP 1998-961867	19981203
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002517383	T2	20020618	JP 2000-552100	19981203
NO 2000006117	A	20010201	NO 2000-6117	20001201
US 2002045641	A1	20020418	US 2001-776904	20010206
PRAI US 1998-87843P	P	19980603		
US 1998-204238	A3	19981203		
WO 1998-US25574	W	19981203		

OS MARPAT 132:18814
RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 10 OF 12 CAPLUS COPYRIGHT 2002 ACS
AN 1999:784078 CAPLUS
DN 132:22860
TI Preparation of aza-heterocyclic compounds used to treat neurological disorders and hair loss
IN Hamilton, Gregory S.; Norman, Mark H.; Wu, Yong-Qian; Steiner, Joseph P.
PA Guilford Pharmaceuticals Inc., USA; Amgen, Inc.
SO PCT Int. Appl., 96 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 5

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9962881	A1	19991209	WO 1998-US25573	19981203
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW,				

MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR,
TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES,
FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI,
CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

	CA 2333963	AA	19991209	CA 1998-2333963	19981203
	AU 9917081	A1	19991220	AU 1999-17081	19981203
	ZA 9811063	A	20000707	ZA 1998-11063	19981203
	BR 9815920	A	20010220	BR 1998-15920	19981203
	EP 1084107	A1	20010321	EP 1998-961866	19981203
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	JP 2002516905	T2	20020611	JP 2000-552093	19981203
	NO 2000005903	A	20010202	NO 2000-5903	20001121
PRAI	US 1998-87788P	P	19980603		
	US 1998-101077P	P	19980918		
	WO 1998-US25573	W	19981203		

OS MARPAT 132:22860
RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

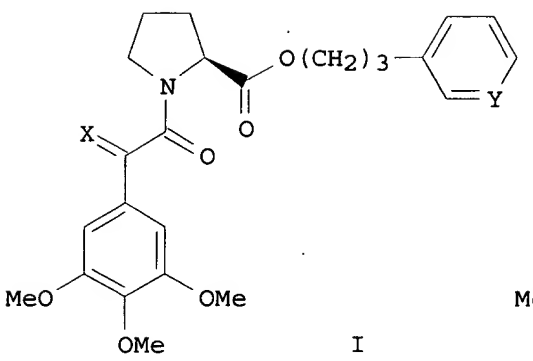
L4 ANSWER 11 OF 12 CAPLUS COPYRIGHT 2002 ACS
AN 1999:784077 CAPLUS
DN 132:18813
TI N-linked sulfonamides of N-heterocyclic carboxylic acids or carboxylic acid isosteres for treatment of neurological disorders and alopecia
IN Hamilton, Gregory S.; Norman, Mark H.; Wu, Yong-Qian
PA Guilford Pharmaceuticals Inc., USA; Amgen, Inc.
SO PCT Int. Appl., 96 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9962880	A1	19991209	WO 1998-US25572	19981203
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	ZA 9811060	A	19991203	ZA 1998-11060	19981203
	CA 2334002	AA	19991209	CA 1998-2334002	19981203
	AU 9917080	A1	19991220	AU 1999-17080	19981203
	EP 1084106	A1	20010321	EP 1998-961865	19981203
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	JP 2002516904	T2	20020611	JP 2000-552092	19981203
	BR 9815882	A	20020917	BR 1998-15882	19981203
	NO 2000006078	A	20010205	NO 2000-6078	20001130
PRAI	US 1998-87842P	P	19980603		
	WO 1998-US25572	W	19981203		

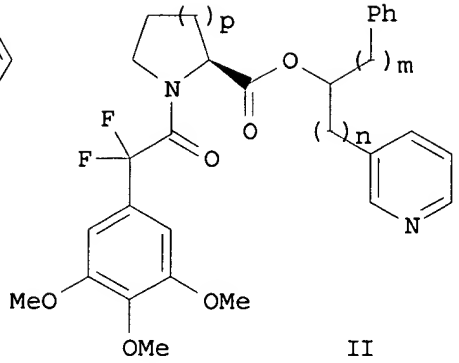
OS MARPAT 132:18813
RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 1 OF 18 CAPLUS COPYRIGHT 2002 ACS
AN 2002:505811 CAPLUS
DN 137:228492
TI Active site residues of cyclophilin A are crucial for its signaling activity via CD147
AU Yurchenko, Vyacheslav; Zybarth, Gabriele; O'Connor, Matthew; Dai, Wei Wei; Franchin, Giovanni; Hao, Tang; Guo, Huiming; Hung, Hsiu-Cheng; Toole, Bryan; Gallay, Philippe; Sherry, Barbara; Bukrinsky, Michael
CS Picower Institute for Medical Research, Manhasset, NY, 11030, USA
SO Journal of Biological Chemistry (2002), 277(25), 22959-22965
CODEN: JBCHA3; ISSN: 0021-9258
PB American Society for Biochemistry and Molecular Biology
DT Journal
LA English
AB Cyclophilin A (CyPA), a ubiquitously distributed intracellular protein, is a peptidylprolyl cis-trans-isomerase and the major target of the potent immunosuppressive drug cyclosporin A. Although expressed predominantly as an intracellular mol., CyPA is secreted by cells in response to inflammatory stimuli and is a potent neutrophil and eosinophil chemoattractant in vitro and in vivo. The mechanisms underlying CyPA-mediated signaling and chemotaxis are unknown. Here, we identified CD147 as a cell surface receptor for CyPA and demonstrated that CD147 is an essential component in the CyPA-initiated signaling cascade that culminates in ERK activation. Both signaling and chemotactic activities of CyPA depended also on the presence of heparans, which served as primary binding sites for CyPA on target cells. The **proline** 180 and glycine 181 residues in the extracellular domain of CD147 were crit. for signaling and chemotactic activities mediated by CD147. Also crucial were active site residues of CyPA, because **rotamase**-defective CyPA mutants failed to initiate signaling events. These results establish cyclophilins as natural ligands for CD147 and suggest an unusual, **rotamase**-dependent mechanism of signaling.
RE.CNT 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 2 OF 18 CAPLUS COPYRIGHT 2002 ACS
AN 2001:836875 CAPLUS
DN 136:118718
TI 2-Aryl-2,2-difluoroacetamide FKBP12 Ligands: Synthesis and X-ray Structural Studies
AU Dubowchik, Gene M.; Vrudhula, Vivekananda M.; Dasgupta, Bireshwar; Ditta, Jonathan; Chen, Ti; Sheriff, Steven; Sipman, Karin; Witmer, Mark; Tredup, Jeffrey; Vyas, Dolatrai M.; Verdoorn, Todd A.; Bollini, Sagarika; Vinitsky, Alexander
CS Bristol-Myers Squibb Pharm. Res. Inst., Wallingford, CT, 06492-7660, USA
SO Organic Letters (2001), 3(25), 3987-3990
CODEN: ORLEF7; ISSN: 1523-7060
PB American Chemical Society
DT Journal
LA English
GI



I



II

AB 2-Aryl-2,2-difluoroacetamido derivs. of **proline** and pipecolate esters I (X = F2, O, H2; Y = N, CH) and II (p = 1, 2; n = 2, 3; m = 0-3) are high affinity FKBP12 ligands whose **rotamase** inhibitory activity is comparable to that seen for the corresponding ketoamides. X-ray structural studies suggest that the fluorine atoms participate in discrete interactions with the Phe36 Ph ring and the Tyr26 hydroxyl group, with the latter resembling a moderate-to-weak hydrogen bond.

RE.CNT 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 3 OF 18 CAPLUS COPYRIGHT 2002 ACS
AN 2000:553538 CAPLUS
DN 133:150911
TI Preparation of carboxylic acid derivatives as rotamase enzyme inhibitors
IN Brumby, Thomas; McDonald, Fiona; Ottow, Eckhard; Schneider, Herbert
PA Schering Aktiengesellschaft, Germany; Vertex Pharmaceuticals, Inc.
SO PCT Int. Appl., 38 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000046181	A1	20000810	WO 2000-US2774	20000203
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	DE 19905255	A1	20000810	DE 1999-19905255	19990203
PRAI	DE 1999-19905255	A	19990203		
	US 1999-126009P	P	19990324		
	US 2000-495478	A	20000201		

OS MARPAT 133:150911
AB Carboxylic acid derivs. R1-Y-NR2CRR3CO-X-R4 [R = alkyl; R1 = H, Ar [Ar is a mono- or bicyclic arom. compd., which can contain 0-4 N, S or O atoms and which optionally is partially hydrogenated and can be substituted in one to three places with E (E = halo, OH, NO2, CF3, CN, OCF3, amino, Ph, methylenedioxy, phenoxy, benzyloxy, alkoxy, alkyl)], alkyl, alkenyl, cycloalkyl, or cycloalkenyl which can be substituted with Ar or E; Y = COCO, SO2, CONH, C(S)NH, COCO2, COCONH, CO2, SO2NH; R2 = alkyl which can be substituted with Ph or halophenyl; R3 = alkyl, alkenyl, cycloalkyl, cycloalkenyl, or cyclohexylmethyl which may be substituted by Ar or R2 and

R3 together with the N atom form a heterocycle which can be satd. or unsatd. and which can be substituted with alkyl or OH; X = O, S, NH, NR5 or a direct bond; R4, R5 = Ar, alkyl, alkenyl, cycloalkyl, cycloalkenyl, where the alkyl and alkenyl radical can be substituted by Ar, cycloalkyl and cycloalkenyl] were prepd. as rotamase enzyme inhibitors. Thus, 3-(3-pyridyl)propyl (2S)-1-(3,3-dimethyl-2-oxovaleroyl)-2-methyl-2-pyrrolidinecarboxylate was prepd. by esterification of Boc-.alpha.-methylproline (Boc = tert-butoxycarbonyl) with 3-(3-pyridyl)-1-propanol, followed by cleavage of the protective group, acylation with Me oxalyl chloride, and addn. reaction with 1,1-dimethylpropylmagnesium chloride.

RE.CNT 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 4 OF 18 CAPLUS COPYRIGHT 2002 ACS
AN 1999:783930 CAPLUS
DN 132:23195
TI Preparation of neurotrophic amino acid difluoroamide agents
IN Vrudhula, Vivekananda M.; Dubowchik, Gene M.; Dasgupta, Bireshwar; Vyas, Dolatrai M.
PA Bristol-Myers Squibb Company, USA
SO PCT Int. Appl., 39 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9962511	A1	19991209	WO 1999-US11348	19990521
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	CA 2333997	AA	19991209	CA 1999-2333997	19990521
	AU 9941975	A1	19991220	AU 1999-41975	19990521
	AU 743199	B2	20020124		
	US 6096762	A	20000801	US 1999-316792	19990521
	EP 1087763	A1	20010404	EP 1999-925749	19990521
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	JP 2002516857	T2	20020611	JP 2000-551767	19990521
	US 6239146	B1	20010529	US 2000-590808	20000609
PRAI	US 1998-87642P	P	19980602		
	US 1999-316792	A3	19990521		
	WO 1999-US11348	W	19990521		

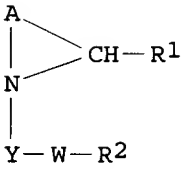
OS MARPAT 132:23195
AB Difluoroamide compds. D-CF2CON(J)CHKCO-W-Z [W = CH2, O, NH, alkylamino; J = H, alkyl, benzyl; K = alkyl, benzyl, cyclohexylmethyl or J and K together may form a heterocyclic ring which may contain O, S, S(O), and SO2 (the stereochem. of the carbon atom at CHK is R or S); Z = Q (H, arylalkyl, alkyl, alkenyl, cycloalkyl, etc.) or -(CH2)mCHQ'A (m = 0-3, Q' and A are H, aryl, alkyl, alkenyl, cycloalkyl, etc.); D = alkyl, alkenyl, cyloalkyl, aryl, etc.] were prepd. as peptidyl-prolyl isomerase (PPIase or rotamase) inhibitors. Thus, 3,4,5-(MeO)3C6H2CF2CO-L-Pro-O(CH2)3Ph was prepd. and assayed for FKBP12 rotamase inhibitory activity (Ki = 1,300 nM and 97% inhibition at 10 .mu.M).

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

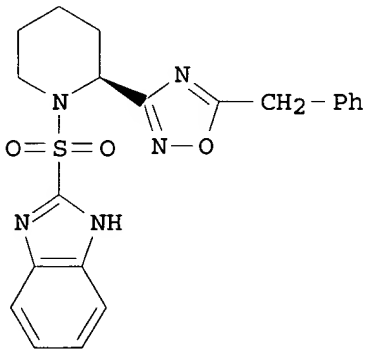
L8 ANSWER 5 OF 18 CAPLUS COPYRIGHT 2002 ACS
AN 1999:576925 CAPLUS
DN 131:214289
TI Preparation of oxadiazolyl piperidine derivatives as rotamase enzyme inhibitors
IN Bull, David John; MaGuire, Robert John; Palmer, Michael John; Wythes, Martin James
PA Pfizer Inc., USA; Pfizer Ltd.
SO PCT Int. Appl., 237 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9945006	A1	19990910	WO 1999-IB259	19990215
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	CA 2322442	AA	19990910	CA 1999-2322442	19990215
	AU 9921810	A1	19990920	AU 1999-21810	19990215
	BR 9908480	A	20001205	BR 1999-8480	19990215
	EP 1060178	A1	20001220	EP 1999-901847	19990215
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
	JP 2002505329	T2	20020219	JP 2000-534548	19990215
PRAI	GB 1998-4426	A	19980302		
	WO 1999-IB259	W	19990215		

OS MARPAT 131:214289
GI



I



II

AB Oxadiazolyl piperidine derivs. and analogs (I) [R1 = 5- or 6-membered heteroaryl (un)substituted ring contg. 1-4 N, or 1 S or O and/or 1-2 N atoms; R2 = H, (un)substituted Ph, (un)substituted C3-7 cycloalkyl, or 5-, 6-, or 7-membered (un)substituted heterocycle; A = C3-5 alkylene; W = direct link, C1-6 alkylene, or C2-6 alkenylene; X = direct link, C1-6 alkylene, or alkylene-Z-alkylene; Y = SO2, CO, (un)substituted CO-NH, CO-CO, CH2-CO, CS-CO, CO-CS, or CO-CH(OH); Z = O, S, (un)substituted CH2-NH, CH(aryl), NH, NH-CO2, CO-NH, or NH-CO] were prepd. as rotamase enzyme inhibitors, particularly FKBP-12 and FKBP-52 inhibitors, to

moderate neuronal regeneration and outgrowth. Thus, ethyldiisopropylamine was added to a mixt. of 5-benzyl-3-[(2S)-2-piperidyl]-1,2,4-oxadiazole hydrochloride (prepn. given) and 1H-benzo[d]imidazole-2-sulfonyl chloride (prepn. given) in CH2Cl2 and the mixt. was stirred for 18 h to yield 1H-benzo[d]imidazol-2-yl [(2S)-2-(5-benzyl-1,2,4-oxadiazol-3-yl)-1-piperidyl] sulfone (II). Seven compds. of the invention were tested for in vitro inhibitory activity against the FKBP-12 enzyme in a coupled colorimetric PPlase assay, and exhibited IC50 values in the range of 81 nm to 2010 nm. One compd. was assayed for inhibitory activity against the FKBP-52 enzyme and gave a Ki value of 685. The compds. are claimed to be useful in treating neurol. disorders arising from neurodegenerative diseases and nerve damage.

RE.CNT 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 6 OF 18 CAPLUS COPYRIGHT 2002 ACS
AN 1999:39083 CAPLUS
DN 130:206459
TI Specific interaction between bovine cyclophilin A and synthetic analogs of cyclolinopeptide A
AU Gallo, Pasquale; Rossi, Filomena; Saviano, Michele; Pedone, Carlo; Colonna, Giovanni; Ragone, Raffaele
CS Centro di Studio di Biocristallografia del C.N.R., Dipartimento di Chimica, Universita degli Studi di Napoli "Federico II,", Naples, 80134, Italy
SO Journal of Biochemistry (Tokyo) (1998), 124(5), 880-885
CODEN: JOBIAO; ISSN: 0021-924X
PB Japanese Biochemical Society
DT Journal
LA English
AB Like cyclosporin A, cyclolinopeptide A binds specifically bovine cyclophilin A, inhibiting its peptidyl-prolyl cis-trans isomerase activity. We describe here the protein interaction with several synthetic analogs of cyclolinopeptide A, which are either homodetic or disulfide bridged heterodetic cyclopeptides characterized by different ring dimensions, in terms of dissocn. and inhibition consts. evaluated by fluorescence and inhibition of the enzyme activity, resp. Dissocn. consts. from fluorescence expts. are practically identical and about 20-fold lower than for cyclosporin A. On the other hand, inhibition consts. differ from compd. to compd. and are higher than for cyclosporin A. This result is therefore difficult to rationalize, but we would suggest decoupling between binding and inhibitory ability of cyclopeptides. The Pro1 residue of cyclolinopeptide A seems to play a fundamental role in detg. the inhibition of the rotamase activity of cyclophilin A, as the homodetic analog lacking this residue does not show any inhibitory ability. Similarly, heterodetic analogs with a ring size smaller than 7 residues do not display inhibition. We presume that the sequence -Pro-Pro-Phe-Phe- and a ring size of 8 residues for homodetic cyclic peptides could be used as starting points in the targeted synthesis of cyclopeptides able to bind both cyclosporin A and calcineurin. The only peptide showing similar values of the dissocn. and inhibition const. is cyclolinopeptide A. This compd. can be considered a novel model for the mol. design of immunosuppressant drugs.

RE.CNT 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 7 OF 18 CAPLUS COPYRIGHT 2002 ACS
AN 1998:630180 CAPLUS
DN 130:25277
TI Intramolecular Catalysis of Amide Isomerization: Kinetic Consequences of the 5-NH- -Na Hydrogen Bond in Prolyl Peptides
AU Cox, Christopher; Lectka, Thomas
CS Department of Chemistry, Johns Hopkins University, Baltimore, MD, 21218,

USA
SO Journal of the American Chemical Society (1998), 120(41), 10660-10668
CODEN: JACSAT; ISSN: 0002-7863
PB American Chemical Society
DT Journal
LA English
AB The presence of an intramol. hydrogen bond has been proposed to play a key role in the catalysis of amide isomerization by peptidylprolyl isomerases (PPIases), which are highly conserved and ubiquitous **rotamase** enzymes that catalyze the cis-trans isomerization of **proline** residues in peptides and proteins. The authors present kinetic and spectroscopic evidence that indicates the existence of an intramol. hydrogen bond between the prolyl amide nitrogen and the adjacent amidic NH within a five-membered ring (the 5-NH-to-Na hydrogen bond) that is capable of catalyzing **proline** isomerization by up to 260-fold in model prolyl peptides. These results provide the first systematic study of intramol. general-acid-catalyzed amide isomerization.
RE.CNT 66 THERE ARE 66 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 8 OF 18 CAPLUS COPYRIGHT 2002 ACS
AN 1997:412743 CAPLUS
DN 127:132694
TI Structural and functional analysis of the mitotic rotamase Pin1 suggests substrate recognition is phosphorylation dependent
AU Ranganathan, Rama; Lu, Kun Ping; Hunter, Tony; Noel, Joseph P.
CS Structural Biology Laboratory, The Salk Institute for Biological Studies, La Jolla, CA, 92037, USA
SO Cell (Cambridge, Massachusetts) (1997), 89(6), 875-886
CODEN: CELLB5; ISSN: 0092-8674
PB Cell Press
DT Journal
LA English
AB The human **rotamase** or peptidyl-prolyl cis-trans isomerase Pin1 is a conserved mitotic regulator essential for the G2/M transition of the eukaryotic cell cycle. We report the 1.35 .ANG. crystal structure of Pin1 complexed with an AlaPro dipeptide and the initial characterization of Pin1's functional properties. The crystallog. structure as well as pH titrn. studies and mutagenesis of an active site cysteine suggest a catalytic mechanism that includes general acid-base and covalent catalysis during peptide bond isomerization. Pin1 displays a preference for an acidic residue N-terminal to the isomerized **proline** bond due to interaction of this acidic side chain with a basic cluster. This raises the possibility of phosphorylation-mediated control of Pin1-substrate interactions in cell cycle regulation.

L8 ANSWER 9 OF 18 CAPLUS COPYRIGHT 2002 ACS
AN 1996:424815 CAPLUS
DN 125:79949
TI Structure of the amino-terminal core domain of the HIV-1 capsid protein
AU Gitti, Rossitza K.; Lee, Brian M.; Walker, Jill; Summers, Michael F.; Yoo, Sanghee; Sundquist, Wesley I.
CS Howard Hughes Med. Inst., Dep. Chem., Biochem., Univ. Maryland, Baltimore, MD, 21228, USA
SO Science (Washington, D. C.) (1996), 273(5272), 231-235
CODEN: SCIEAS; ISSN: 0036-8075
PB American Association for the Advancement of Science
DT Journal
LA English
AB The three-dimensional structure of the amino-terminal core domain (residues 1 through 151) of the human immunodeficiency virus-type 1 (HIV-1) capsid protein has been solved by multidimensional heteronuclear magnetic resonance spectroscopy. The structure is unlike those of

previously characterized viral coat proteins and is composed of seven .alpha. helixes, two .beta. hairpins, and an exposed partially ordered loop. The domain is shaped like an arrowhead, with the .beta. hairpins and loop exposed at the trailing edge and the carboxyl-terminal helix projecting from the tip. The **proline** residue Pro1 forms a salt bridge with a conserved, buried aspartate residue (Asp51), which suggests that the amino terminus of the protein rearranges upon proteolytic maturation. The binding site for cyclophilin A, a cellular **rotamase** that is packaged into the HIV-1 virion, is located on the exposed loop and encompasses the essential **proline** residue Pro90. In the free monomeric domain, Pro90 adopts kinetically trapped cis and trans conformations, raising the possibility that cyclophilin A catalyzes interconversion of the cis- and trans-Pro90 loop structures.

L8 ANSWER 10 OF 18 CAPLUS COPYRIGHT 2002 ACS
AN 1996:321486 CAPLUS
DN 125:5097
TI Immunophilins in the yeast Saccharomyces cerevisiae: a different spin on **proline rotamases**
AU Dhillon, Namrita; Thorner, Jeremy
CS Dep. Molecular Cell Biology, Univ. California, Berkeley, CA, 94720-3202, USA
SO Methods (San Diego) (1996), 9(2), 165-176
CODEN: MTHDE9; ISSN: 1046-2023
PB Academic
DT Journal; General Review
LA English
AB A review with 114 refs. Clin. used immunosuppressant compds. - FK506, rapamycin, and cyclophilin A - are all natural products that were originally detected because of their antifungal action, not because of their fortuitous effects on the human immune system. Genetic and biochem. approaches have been used to identify binding proteins that serve as the receptors for these antibiotics in cells of the budding yeast Saccharomyces cerevisiae. Three FK506/rapamycin-binding proteins (FKBPs) and six cyclosporin A-binding proteins (cyclophilins) have been characterized in some detail, but there is evidence that addnl. members of both families exist in this organism. Cloning of the corresponding genes has shown that the yeast gene products are strikingly similar to their mammalian counterparts and possess peptidyl-prolyl-cis,trans-isomerase (**proline rotamase**) activity in vitro. Genetic anal. in yeast has confirmed, and significantly extended, complementary research in animal cell systems that has shed light on the roles that the FKBPs and the cyclophilins play in the mechanism of action of the immunosuppressant drugs. The application of genetic methods in yeast is also beginning to provide addnl. insights into the function of these proteins in normal cell physiol.

L8 ANSWER 11 OF 18 CAPLUS COPYRIGHT 2002 ACS
AN 1996:315749 CAPLUS
DN 125:28759
TI Catalytic Antibodies with Peptidyl-Prolyl Cis-Trans Isomerase Activity
AU Yli-Kauhaluoma, Jari T.; Ashley, Jon A.; Lo, Chih-Hung L.; Coakley, Julie; Wirsching, Peter; Janda, Kim D.
CS Scripps Research Institute, La Jolla, CA, 92037, USA
SO Journal of the American Chemical Society (1996), 118(23), 5496-5497
CODEN: JACSAT; ISSN: 0002-7863
PB American Chemical Society
DT Journal
LA English
AB The mechanism of the immunophilin peptidyl-prolyl isomerases has not been completely established. The work of others led to the hypothesis that the dicarbonyl moiety in peptide-like immunophilin ligands was a twisted-amide mimetic. To examine the possible influence of this functionality in

catalysis, a tripeptide analog contg. an .alpha.-ketoamide bond to the nitrogen of **proline** was used as a hapten to elicit antibodies having **rotamase** activity. A panel of 28 monoclonal antibodies (mAbs) was obtained of which 2 increased the rate of P1-prolyl cis to trans isomerization of tripeptide substrates. The mAbs operated with high substrate specificity and gave rate enhancements up to 27-fold over the spontaneous interconversion. In light of the hydrophobic nature of the peptides and data from kinetic and binding studies, it was concluded that the programming of the antibody site by the .alpha.-ketoamide hapten afforded both desolvation effects and geometric constraints that played a role in catalysis.

L8 ANSWER 12 OF 18 CAPLUS COPYRIGHT 2002 ACS
AN 1995:891557 CAPLUS
DN 123:280465
TI The yeast immunophilin Fpr3 is a physiological substrate of the tyrosine-specific phosphoprotein phosphatase Ptp1
AU Wilson, Linda K.; Benton, Bret M.; Zhou, Sharleen; Thorner, Jeremy; Martin, G. Steven
CS Div. Biochem. Mol. Biol., Univ. California, Berkeley, CA, 94720-3204, USA
SO Journal of Biological Chemistry (1995), 270(42), 25185-93
CODEN: JBCHA3; ISSN: 0021-9258
PB American Society for Biochemistry and Molecular Bio logy
DT Journal
LA English
AB The tyrosine-specific phosphoprotein phosphatase encoded by the Saccharomyces cerevisiae PTP1 gene dephosphorylates artificial substrates in vitro, but little is known about its functions and substrates in vivo. The presence of Ptp1 resulted in dephosphorylation of multiple tyrosine-phosphorylated proteins in yeast expressing a heterologous tyrosine-specific protein kinase, indicating that Ptp1 can dephosphorylate a broad range of substrates in vivo. Correspondingly, several proteins phosphorylated at tyrosine by endogenous protein kinases exhibited a marked increase in tyrosine phosphorylation in ptp1 mutant cells. One of these phosphotyrosyl proteins (p70) was also dephosphorylated in vitro when incubated with recombinant Ptp1. Protein p70 was purified to homogeneity; anal. of four tryptic peptides revealed that p70 is identical to the recently described FPR3 gene product, a nucleolarly localized **proline rotamase** of the FK506- and rapamycin-binding family. The identity of p70 with Fpr3 was confirmed in the demonstration that the abundance of tyrosine-phosphorylated p70 in ptp1 mutants was strictly correlated with the level of FPR3 expression; immobilized phosphotyrosyl Fpr3 was directly dephosphorylated by recombinant Ptp1. Site-directed mutagenesis demonstrated that the site of tyrosine phosphorylation is Tyr-184, which resides within the nucleolin-like amino-terminal domain of Fpr3. Protein kinase activities from yeast cell exts. can bind to and phosphorylate the immobilized amino-terminal domain of Fpr3 on serine, threonine, and tyrosine. Fpr3 represents the first phosphotyrosyl protein identified in S. cerevisiae that is not itself a protein kinase and is as yet the only known physiol. substrate of Ptp1.

L8 ANSWER 13 OF 18 CAPLUS COPYRIGHT 2002 ACS
AN 1994:673586 CAPLUS
DN 121:273586
TI A novel FK506- and rapamycin-binding protein (FPR3 gene product) in the yeast Saccharomyces cerevisiae is a **proline rotamase** localized to the nucleolus
AU Benton, Bret M.; Zang, Ji-Hong; Thorner, Jeremy
CS Dep. Molecular Cell Biology, Univ. California, Berkeley, CA, 94720-3202, USA
SO Journal of Cell Biology (1994), 127(3), 623-39
CODEN: JCLBA3; ISSN: 0021-9525
DT Journal

LA English
AB The gene (FPR3) encoding a novel type of peptidylprolyl-cis-trans-isomerase (PPIase) was isolated during a search for previously unidentified nuclear proteins in Saccharomyces cerevisiae. PPIases are thought to act in conjunction with protein chaperones because they accelerate the rate of conformational interconversions around proline residues in polypeptides. The FPR3 gene product (Fpr3) is 413 amino acids long. The 111 COOH-terminal residues of Fpr3 share greater than 40% amino acid identity with a particular class of PPIases, termed FK506-binding proteins (FKBPs) because they are the intracellular receptors for two immunosuppressive compds., rapamycin and FK506. When expressed in and purified from Escherichia coli, both full-length Fpr3 and its isolated COOH-terminal domain exhibit readily detectable PPIase activity. Both fpr3.DELTA. null mutants and cells expressing FPR3 from its own promoter on a multicopy plasmid have no discernible growth phenotype and do not display any alteration in sensitivity to the growth-inhibitory effects of either FK506 or rapamycin. In S. cerevisiae, the gene for a 112-residue cytosolic FKBP (FPR1) and the gene for a 135-residue ER-assocd. FKBP (FPR2) have been described before. Even fpr1 fpr2 fpr3 triple mutants are viable. However, in cells carrying an fpr1.DELTA. mutation (which confers resistance to rapamycin), overexpression from the GAL1 promoter of the C-terminal domain of Fpr3, but not full-length Fpr3, restored sensitivity to rapamycin. Conversely, overprodn. from the GAL1 promoter of full-length Fpr3, but not its COOH-terminal domain, is growth inhibitory in both normal cells and fpr1.DELTA. mutants. In fpr1.DELTA. cells, the toxic effect of Fpr3 overprodn. can be reversed by rapamycin. Overprodn. of the NH2-terminal domain of Fpr3 is also growth inhibitory in normal cells and fpr1.DELTA. mutants, but this toxicity is not ameliorated in fpr1.DELTA. cells by rapamycin. The NH2-terminal domain of Fpr3 contains long stretches of acidic residues alternating with blocks of basic residues, a structure that resembles sequences found in nucleolar proteins, including S. cerevisiae NSR1 and mammalian nucleolin. Indirect immunofluorescence with polyclonal antibodies raised against either the NH2- or the COOH-terminal segments of Fpr3 expressed in E. coli demonstrated that Fpr3 is located exclusively in the nucleolus.

L8 ANSWER 14 OF 18 CAPLUS COPYRIGHT 2002 ACS
AN 1994:72242 CAPLUS
DN 120:72242
TI A mechanism for rotamase catalysis by the FK506 binding protein (FKBP)
AU Fischer, Stefan; Michnick, Stephen; Karplus, Martin
CS Dep. Chem., Harvard Univ., Cambridge, MA, 02138, USA
SO Biochemistry (1993), 32(50), 13830-7
CODEN: BICHAW; ISSN: 0006-2960
DT Journal
LA English
AB A detailed mechanism for the catalysis of prolyl isomerization by the **rotamase** enzyme FKBP is proposed on the basis of a model constructed from the known structure of the FK506/FKBP complex. The model substrate is bound as a type VIa **proline** turn with the ends exposed to permit longer polypeptide chains (e.g., protein loops) to act as substrates. An ab initio potential for the isomerized imide bond is combined with a mol. mechanics representation of the rest of the system to calc. the reaction path. The resulting activation energy for the enzymic cis .fwdarw. trans isomerization is equal to about 6 kcal/mol, in good agreement with expt. The lowering of the barrier relative to the soln. value of 19 kcal/mol is found to arise from a combination of desolvation of the imide carbonyl, ground-state destabilization, substrate autocatalysis, and preferential transition-state binding. Minimal rearrangements are required in the enzyme and the substrate along the reaction path. The enzyme residues that participate in catalysis agree with the available mutation data. The type VIa turn model corresponds to a sequence-specific structural motif commonly found on the surface of

proteins. It is likely to have a role in the formation of protein complexes with FKBP-like domains that function as foldases or chaperones.

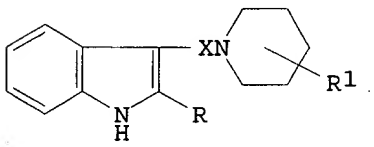
L8 ANSWER 15 OF 18 CAPLUS COPYRIGHT 2002 ACS
AN 1994:3411 CAPLUS
DN 120:3411
TI Mechanism for the rotamase activity of FK506 binding protein from molecular dynamics simulations
AU Orozco, Modesto; Tirado-Rives, Julian; Jorgensen, William L.
CS Dep. Chem., Yale Univ., New Haven, CT, 06511-8118, USA
SO Biochemistry (1993), 32(47), 12864-74
CODEN: BICHAW; ISSN: 0006-2960
DT Journal
LA English
AB Mol. dynamics (MD) and free energy perturbation (FEP) methods are used to study the binding and mechanism of isomerization of a tetrapeptide (AcAAPFNMe) by FK506 binding protein (FKBP). Detailed structures are predicted for the complexes of FKBP with the peptide in both ground-state and transition-state forms. The results support a mechanism of catalysis by distortion, where a large no. of nonbonded interactions act together to stabilize preferentially the twisted transition state. The two most important groups for the catalysis are suggested to be Trp59 and Asp37, but several other groups are identified as directly or indirectly involved in the binding and catalysis. However, the structural results do not support, the notion that the keto oxygen of the immunosuppressive agents FK506 and rapamycin mimics the oxygen for the twisted peptide bond in the FKBP-transition-state complex.

L8 ANSWER 16 OF 18 CAPLUS COPYRIGHT 2002 ACS
AN 1991:579201 CAPLUS
DN 115:179201
TI Targets for cell cycle arrest by the immunosuppressant rapamycin in yeast
AU Heitman, Joseph; Movva, N. Rao; Hall, Michael N.
CS Biocent., Univ. Basel, Basel, CH-4056, Switz.
SO Science (Washington, DC, United States) (1991), 253(5022), 905-9
CODEN: SCIEAS; ISSN: 0036-8075
DT Journal
LA English
AB FK506 and rapamycin are related immunosuppressive compds. that block helper T cell activation by interfering with signal transduction. In vitro, both drugs bind and inhibit the FK506-binding protein (FKBP) **proline rotamase**. Saccharomyces cerevisiae cells treated with rapamycin irreversibly arrested in the G1 phase of the cell cycle. An FKBP-rapamycin complex is concluded to be the toxic agent because (i) strains that lack FKBP **proline rotamase**, encoded by FPR1, were viable and fully resistant to rapamycin and (ii) FK506 antagonized rapamycin toxicity in vivo. Mutations that conferred rapamycin resistance altered conserved residues in FKBP that are crit. for drug binding. Two genes other than FPR1, named TOR1 and TOR2, that participate in rapamycin toxicity were identified. Nonallelic noncomplementation between FPR1, TOR1, and TOR2 alleles suggests that the products of these genes may interact as subunits of a protein complex. Such a complex may mediate nuclear entry of signals required for progression through the cell cycle.

L8 ANSWER 17 OF 18 CAPLUS COPYRIGHT 2002 ACS
AN 1991:576301 CAPLUS
DN 115:176301
TI FK 506-binding protein **proline rotamase** is a target for the immunosuppressive agent FK 506 in Saccharomyces cerevisiae
AU Heitman, Joseph; Movva, N. Rao; Hiestand, Peter C.; Hall, Michael N.
CS Biocent., Univ. Basel, Basel, CH-4056, Switz.
SO Proceedings of the National Academy of Sciences of the United States of

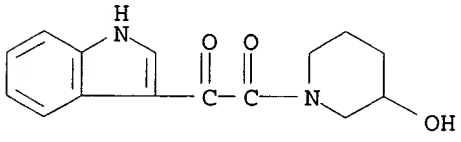
America (1991), 88(5), 1948-52
CODEN: PNASA6; ISSN: 0027-8424
DT Journal
LA English
AB FK 506 and cyclosporin A are potent immunosuppressive compds. that inhibit T-cell activation by interfering with signal transduction. In vitro, FK 506 binds and inhibits the activity of FK 506-binding protein (FKBP), a peptidylprolyl **rotamase** (cis-trans isomerase). Cyclosprorin A acts similarly on a different **proline rotamase**, cyclophilin. Expts. described here demonstrate genetically that FKBP is a target for FK 506 in vivo. The gene encoding the FKBP **proline rotamase** (FPR1) was isolated from Saccharomyces cerevisiae. The encoded yeast protein is highly homologous with bovine and human FKBP and shares no homol. with cyclophilin. Disruption of FPR1 and CPR1 (encoding cyclophilin) individually or in combination is not lethal; thus, either enzymic **proline** rotamerization is not essential for life or an unknown **proline rotamase** can substitute for the missing enzymes. Overexpression or disruption of FPR1 confers resistance to growth inhibition by FK 506, suggesting that FKBP is a target for FK 506 in yeast. However, FKBP is only one of at least two targets because strains lacking FKBP are only partially resistant to FK 506.

AN 1981:47062 CAPLUS
DN 94:47062
TI Synthesis and cardiovascular activity of piperidylethylindoles
AU Agarwal, Jagdish C.; Sharma, M.; Saxena, A. K.; Kishor, K.; Bhargava, K. P.; Shanker, K.
CS Dep. Pharmacol. Ther., King George's Med. Coll., Lucknow, India
SO Journal of the Indian Chemical Society (1980), 57(7), 742-3
CODEN: JICSAH; ISSN: 0019-4522
DT Journal
LA English
GI

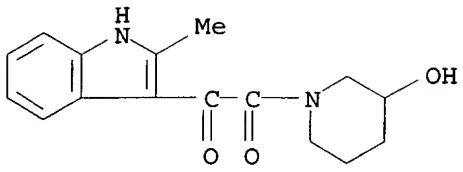


I, X=CH_2CH_2
II, X=COCO

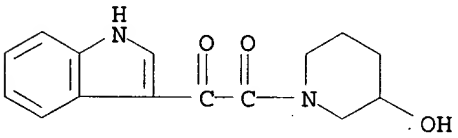
AB The piperidinoethylindoles I (R = H, Me, Ph; R1 = 2-Me, 3-Me, 4,4-Ph, HO) were prepd. by reaction of the corresponding piperidine with indoleglyoxylyl chloride to give II which were reduced with LiAlH4 to give I. Three compds. showed mild hypotensive activity and 2 compds. produced a short lasting hypertensive effect.
IT **71765-50-9P 71765-53-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and redn. of)
RN 71765-50-9 CAPLUS
CN 3-Piperidinol, 1-(1H-indol-3-yloxoacetyl)- (9CI) (CA INDEX NAME)



RN 71765-53-2 CAPLUS
CN 3-Piperidinol, 1-[(2-methyl-1H-indol-3-yl)oxoacetyl]- (9CI) (CA INDEX NAME)



L4 ANSWER 6 OF 7 CAPLUS COPYRIGHT 2002 ACS
AN 1979:568360 CAPLUS
DN 91:168360
TI Pharmacological evaluation of some newer piperidyl ethyl indoles as anti-parkinsonian agent
AU Agarwal, Jagdish C.; Nath, C.; Sharma, M.; Kishor, K.; Shanker, K.; Gupta, G. P.; Bhargava, K. P.
CS Dep. Pharmacol. Ther., King George's Med. Coll., Lucknow, India
SO Indian Drugs (1979), 16(9), 209-12
CODEN: INDRBA; ISSN: 0019-462X
DT Journal
LA English
AB The antiparkinsonian and analgesic activities and the effects on locomotor activities of 23 indole derivs. were studied in rats and mice, and among these, 4 compds. antagonized oxotremorine-induced tremors, 10 antagonized reserpine-induced rigidity, and 1 decreased the locomotor activity, while 2 increased it. Only 2 compds. showed mild analgesic activity.
IT **71765-50-9 71765-53-2**
RL: BIOL (Biological study)
(as antiparkinsonian drug)
RN 71765-50-9 CAPLUS
CN 3-Piperidinol, 1-(1H-indol-3-yloxoacetyl)- (9CI) (CA INDEX NAME)



RN 71765-53-2 CAPLUS
CN 3-Piperidinol, 1-[(2-methyl-1H-indol-3-yl)oxoacetyl]- (9CI) (CA INDEX NAME)